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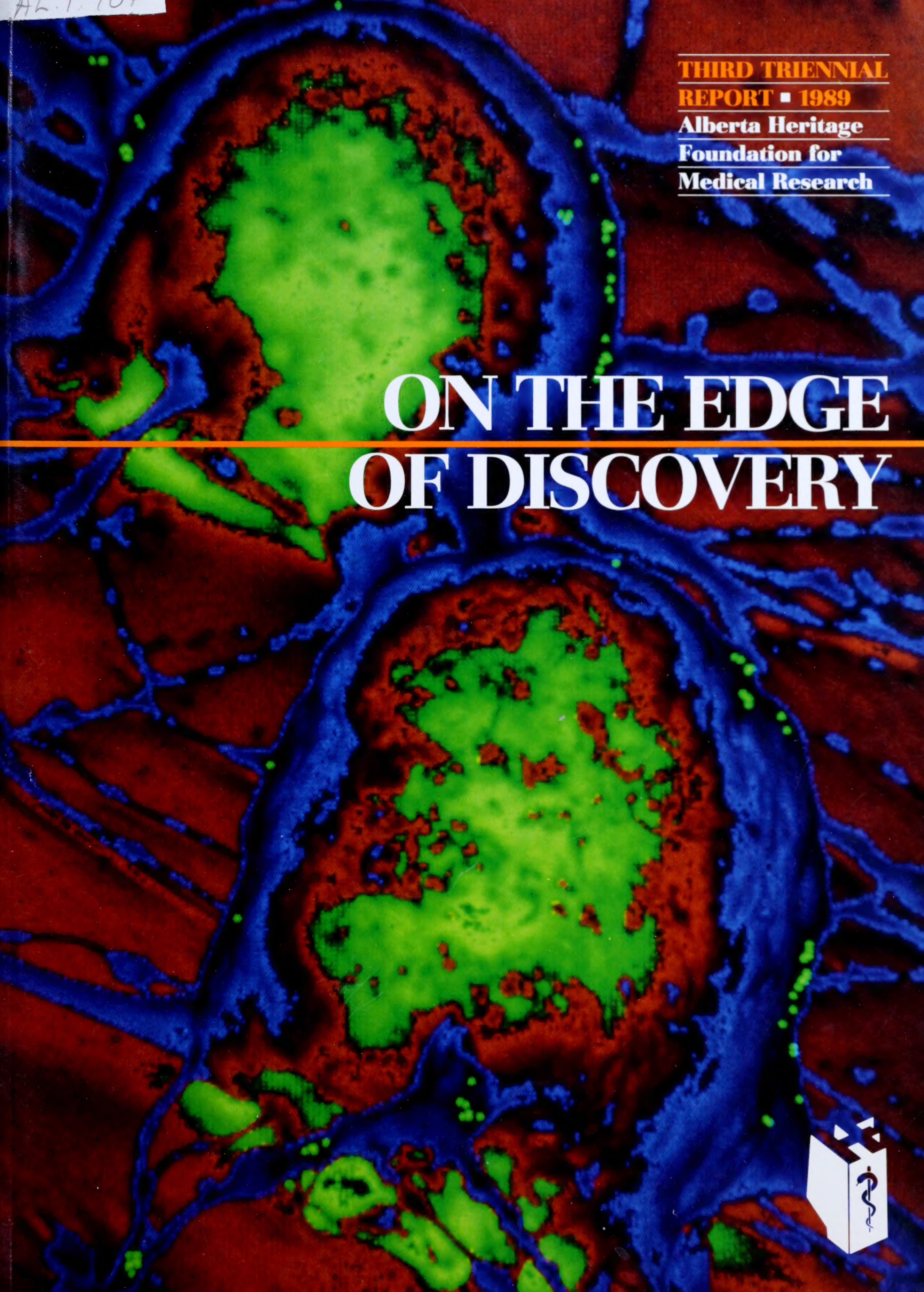

THIRD TRIENNIAL
REPORT ▪ 1989

Alberta Heritage
Foundation for
Medical Research

ON THE EDGE
OF DISCOVERY

Alberta Heritage
Foundation for
Medical Research

3125 ManuLife Place
10180 - 101 Street
Edmonton, Alberta
T5J 3S4
Tel: (403) 423-5727

ON THE EDGE OF DISCOVERY

CANADIANA
NOV 21 1989

Take a Revolution

.....The molecular biology revolution

Add a Vision

.....Alberta as a world centre of medical research

Create a Vehicle

.....The Alberta Heritage Foundation for Medical Research

Acquire the Funds

.....$300 million from Heritage Trust Fund to start

Find the People

.....Scientists from Canada and all over the world

Result:

.....A critical mass of researchers on the edge of discoveries for better health

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Cover photo: "Neuronal Tapestry", a scanning electron micrograph of isolated snail nerve cells magnified 2,000 times.
Photographer: Dr. Robert Berdan (See page 16)

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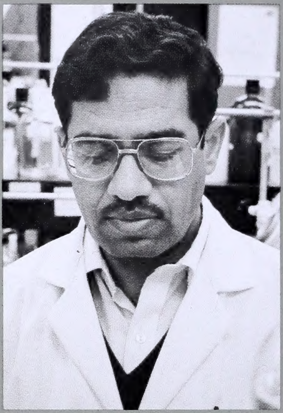
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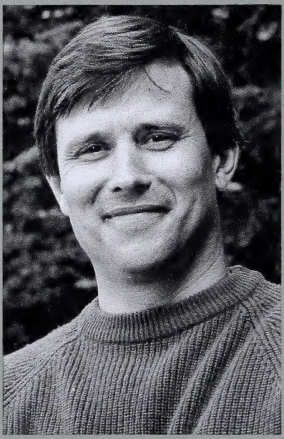
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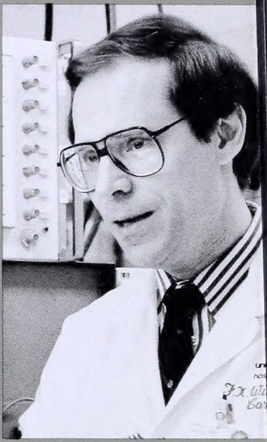
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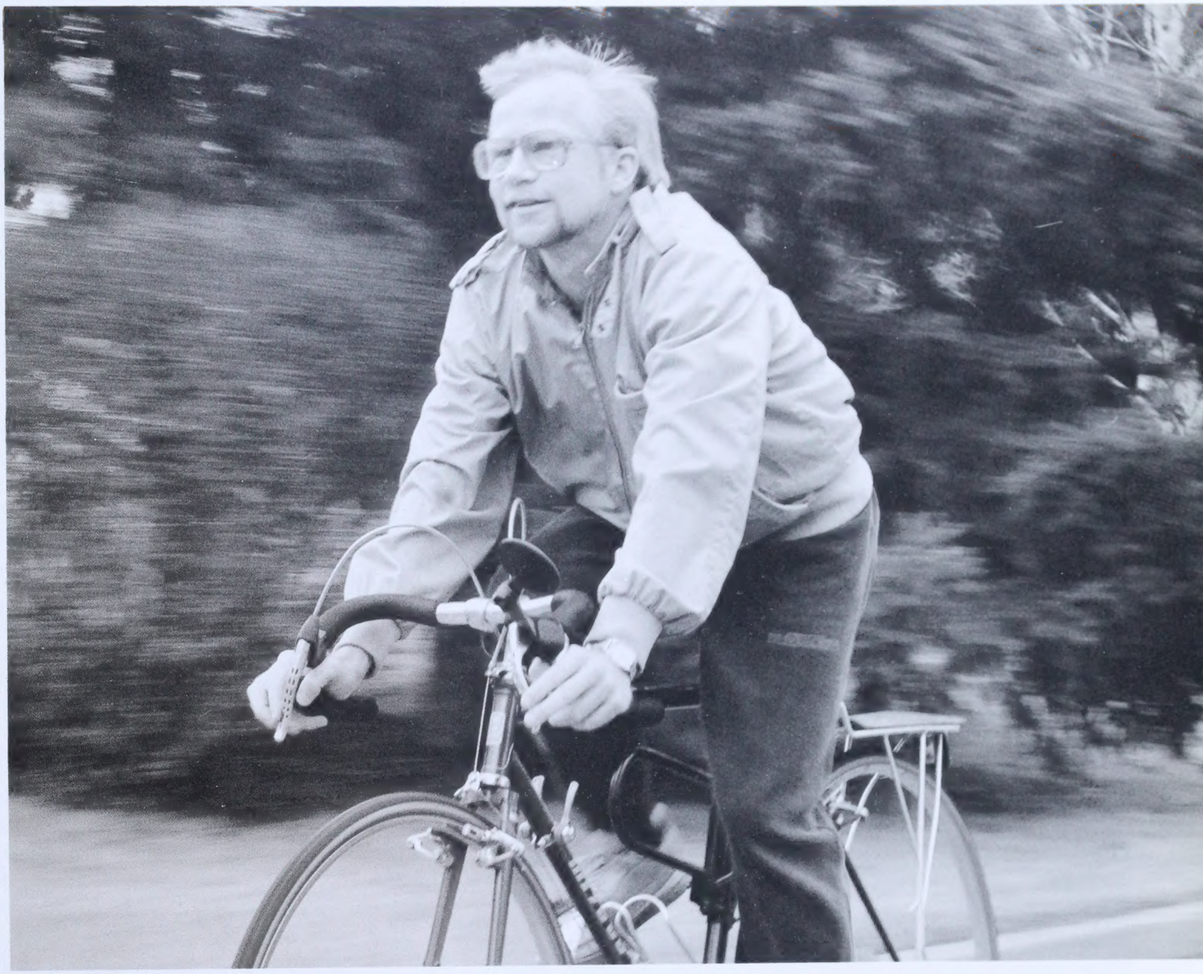
New Hope for Curing Diabetes



In a two and a half week period Jim Connor realized he couldn't see well enough to read anymore. He'd had eye trouble before, but this was much worse. He was going blind.

It was the latest complication of juvenile diabetes, a disease he'd been battling for 15 years, since he was 19. "All of a sudden things went really bad. It was scary," he recalls. Operations on his eyes regained most of his sight, but then his kidneys began failing. This past year he was on ambulatory dialysis using a catheter system he managed himself, rather than a dialysis machine. The procedure took him four hours a day, meant he showered with an IV pole, and it did not eliminate minor health problems with the kidney failure.

On February 23, 1989 Jim's life changed dramatically. That's the day he received a kidney transplant and in the same operation became the first Canadian to receive an islet transplant at the University of Alberta Hospital.

"I feel like a 100 pound weight's been lifted off my back."

Jim Connor

The U of A Islet Transplant Team: (left to right) Dr. Norman Kneteman, Dr. Ray Rajotte, Dr. Garth Warnock

. . . Diabetes

Islets in the pancreas contain the insulin-producing cells which are destroyed in juvenile diabetes. The big question was: would the transplanted islets produce enough insulin to help Jim?

Five weeks later (at the time of publication) Jim was back at work. The kidney was functioning well and the transplanted islets were producing enough insulin that, with a supplement, his blood sugar levels were safely controlled. This was in spite of the fact that a steroid he took for the kidney transplant raised blood sugar levels. Prior to the transplants, insulin supplements couldn't keep Jim out of trouble. When he goes off the steroid, there's a chance he won't need extra insulin at all. After five weeks it's too soon to tell, but Jim's progress is most promising. Blood levels of C-peptide (secreted with insulin from the transplanted islets) indicate Jim no longer fits the strict definition of an insulin-dependent diabetic.

With functioning islets, Jim most likely doesn't need to worry about losing his eyesight again because the progress of the disease is halted. If, as researchers believe is possible, Jim could be insulin-free, the diabetes is reversed.

"Right now I'm just going day by day, and I feel much more energetic," says Jim, adding with a grin, "I feel like a 100 pound weight's been lifted off my back."

U of A Team Leads

Jim's islet transplant was the fruition of years of careful research by a team founded by Dr. Ray Rajotte at the U of A. "It's very exciting and there's a feeling of unreality after all the years of research," says Jim's surgeon, Dr. Garth Warnock. The Foundation sent Dr. Warnock and the third team member, Dr. Norman Kneteman, to the leading labs in Britain and the U.S. to acquire islet transplant expertise.

On their return the team was in a race with researchers around the world working towards the same goal. A number of unsuccessful and partially successful attempts were reported elsewhere, with one Swiss success reported in 1980. The Alberta team believes Jim's operation heralds the beginning of what could be the world's first successful, ongoing islet transplant program.

The U of A team succeeded where others have failed because they spent years perfecting the technology to tackle the problems others experienced. Dr. Rajotte developed cryopreservation methods so the islets can be frozen in a tissue bank. Dr. Kneteman specializes in improving immunosuppressive therapy to reduce the chances of rejection. Dr. Warnock perfected methods of harvesting the islets and purifying them so only a fraction of a mL is necessary for the transplant. All three rely on the expertise of dedicated technicians, Fellows, and other diabetes researchers mainly funded by the Foundation.

Jim's experience gives hope to the 50,000 Canadian children whose juvenile diabetes places them at risk for kidney and heart failure, blindness and peripheral nerve damage. The team is very optimistic, but cautions that this is still an experimental procedure.

"This is just a start," says Dr. Warnock. "All of the information must be carefully interpreted before we can recommend islet transplants be done widely."

Achievements:

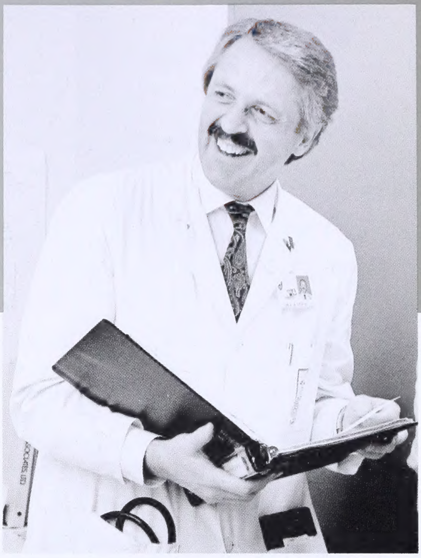
- New therapy for diabetes developed
- Islet transplant program made possible by funding generous enough to provide depth of expertise, training opportunities for physicians and appropriate facilities
- Investment in Alberta's own scientists pays dividends

Challenges:

- To expand clinical trials
- To build an islet program and find funding
- To evaluate cost/benefit ratio of therapy
- To disseminate technology world-wide
- To adequately fund other Alberta scientists with great promise in other areas

Take Heart

> *"What we'd hoped for and wished for is happening. For some people we can prevent a second heart attack and we're on the verge of being able to prevent a heart attack from ever occurring in some people at high risk."*
>
> Dr. George Wyse



A heart attack used to mean sure death—and still does for 30,000 Canadians a year—but physicians are learning how to manage the problem. One key is using drugs to control irregular, rapid heart beats called arrhythmias. The hitch is that the drugs work for some, but not all patients and each individual responds differently to various drugs.

Researchers at The University of Calgary Cardiac Group, headed by Dr. George Wyse, are developing new ways to determine which drugs are effective for a patient and are discovering new alternatives for those patients who cannot be helped by drugs at all. Equally important, they're pioneering new ways to identify people whose arrhythmias place them at high risk for sudden cardiac death, so that it might be prevented with new drug therapy.

"Our whole approach to the problem of heart attack is startlingly different than it was even five years ago.... Then we said, 'We really can't do anything for you, but we'll keep you in the hospital for awhile and put out any fires'. Now we start doing things to help patients as soon as they come in the door. Our whole attitude has changed because now we can make a difference," says Dr. Wyse.

Advancements by the team are numerous. They have a custom-designed system to map heart activity throughout the body. They've developed and tested a new method to try various antiarrhythmia drugs under specially controlled conditions simulating a heart attack. This allows physicians to determine if any drugs will work for individual patients before an attack occurs. They've developed and tested new drugs and new combinations of drugs.

This success can be traced to a creative group where some people work directly with patients; some work with cells, molecules and animals in the lab to understand the basic mechanisms of heart action and drug therapy; and some people do both.

Dr. Wyse comments, "The difference has been clearly the opportunity to bring together a group of individuals working in a particular area. I don't believe there is a group anywhere that's as well-qualified to focus on this problem.... We stack up favourably against arrhythmia researchers anywhere in the world."

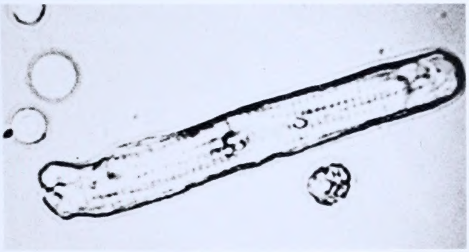
Achievements:

- Established a strong multidisciplinary group of eight researchers covering the spectrum from clinical to basic research
- Developed a strong program of clinical research
- Researchers have pioneered new diagnostic methods, new therapies, new drugs and new devices to treat and prevent sudden cardiac death
- The team has acquired international recognition

Challenges:

- To develop more potent drugs with fewer side effects, using knowledge from basic research
- To establish a wide base of clinical research and communicate results widely to physicians
- To take innovations (therapy and devices) through the technology transfer process

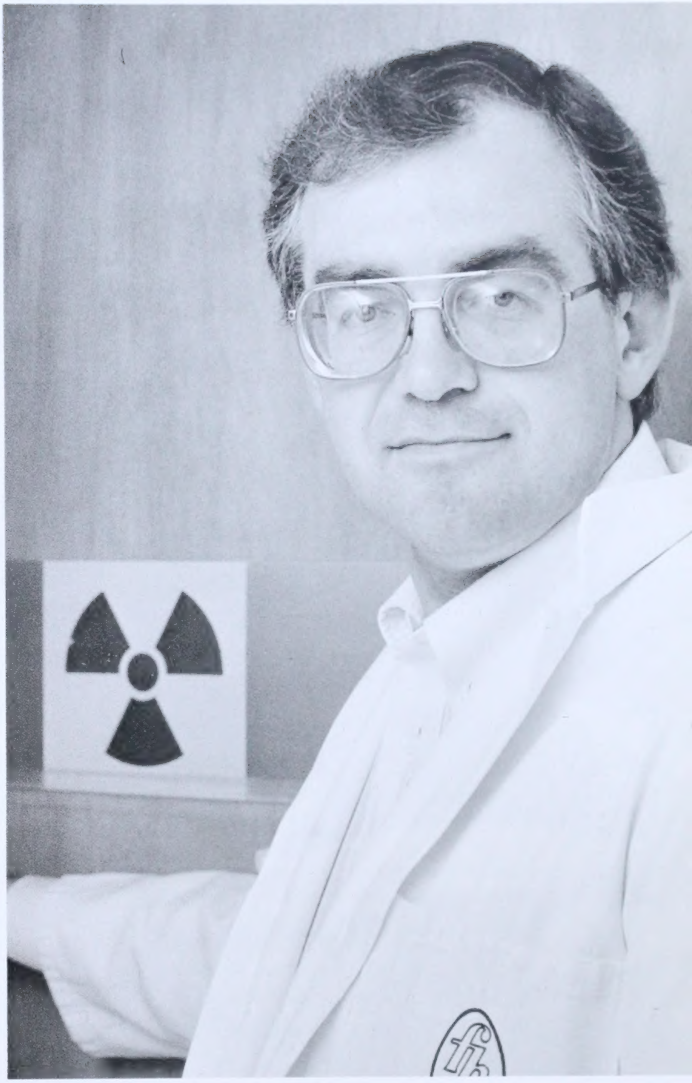
The expertise of the U of C arrhythmia team has been recognized internationally. The group is one of three centres participating in a $65 million international clinical trial for antiarrhythmic drugs run by the prestigious National Institutes of Health in the U.S. Dr. Wyse points out that the size of the study indicates the importance of the problem and his team has contributed significantly to the design and execution of the trials. Calgary is also one of four centres in the world testing the new generation of implanted automatic defibrillators which detect arrhythmias, then give the heart a shock to restore normal rhythms.



This is a single cardiac cell. Your heart contains hundreds of millions of these cells to keep the heart pumping lifeblood over 100,000 times a day! A view of the isolated cardiac cell is as important to the cardiac researcher as the first photos of outer space were to astronauts.

Because he developed the technology to do it, Dr. Wayne Giles is one of the few scientists in the world who can study electrical currents in single cardiac cells to understand how they stimulate the heart to pump and how they respond to cardiac drugs. He feeds this information to physicians such as Dr. Wyse who in turn feed back information about patient response to aid further research.

Other AHFMR cardiac researchers study pump action in the heart. Dr. Henk ter Keurs has new information about how arrhythmias are triggered. Dr. John Tyberg has shown physicians how to more accurately measure pressure on the heart from the sac surrounding it.



Dr. Wayne Giles

Miracle Child

*"Occasionally I think, 'Wow. We did it.
Christopher is here and he's special'."*
Joanne Reimer

Calgarian Joanne Reimer had three consecutive and unexplained miscarriages after bearing a healthy daughter. Joanne and her husband, Tim, had almost given up hope of having a second child until they were referred to Dr. Marvin Fritzler.

Dr. Fritzler discovered Joanne carries lupus autoantibodies in her blood, though she has no clinical signs of the disease. When Joanne became pregnant again Dr. Fritzler prescribed cortisone, a drug used for lupus. She recalls, "We thought this had to be the last chance. It's hard to put yourself through this again. But we felt so comforted to know something could be done this time."

The pregnancy was successful and lively Christopher Reimer was born. After the strain of repeated miscarriages, Joanne and Tim remember well how it felt. "It was like a miracle."

An international authority on the mysterious disease called lupus, Dr. Fritzler has found that repeated, unexplained miscarriages are sometimes due to lupus autoantibodies in the blood. Treatment with aspirin and low doses of cortisone has been 100% successful for the 12 women identified with the problem so far. Lupus is an autoimmune disease (meaning the body attacks its own healthy tissue) and apparently the immune systems of these women are reacting against their fetuses.

Fritzler also suspects lupus autoantibodies may account for unexplained heart attacks and strokes in young women.

Unmasking the Great Imposter

These studies are only one aspect of Dr. Fritzler's research on systemic lupus erythematosus, lupus for short. It's nicknamed The Great Imposter because its symptoms imitate so many diseases, making it difficult to diagnose. Though it varies in each patient, lupus can attack almost any organ particularly the heart, nervous system, kidneys, and lungs. Not surprisingly, many patients have gone undiagnosed or misdiagnosed for years.

Dr. Fritzler has pioneered sophisticated diagnostic techniques which allow physicians to identify lupus in its early stages. Because his methods are more advanced than most others, physicians and researchers from Europe, China, Brazil, the U.S., other parts of Canada, and many other countries send him unusual blood samples to analyze.

Early diagnosis has allowed Calgary physicians to save the lives of lupus babies with heart block (born to women who carry the antibodies but have no lupus symptoms).

The techniques also serve Dr. Fritzler in his search for the cause of lupus and its cure. Presently there is no known cause though hormones, genes, and viruses are implicated. Stress causes flare-ups. Even sunlight may be a factor and might explain why Southern Albertans have a greater incidence than other North Americans. (One in every 500 women of child-bearing age in Southern Alberta has lupus).

Though there is no cure, earlier diagnosis and earlier drug therapy has helped control the disease much better than in past decades. In this way Dr. Fritzler's contributions are advancing treatment. With his combined expertise in molecular biology and patient care he gets closer and closer to tracking down this vicious disease, fittingly named "lupus" after the wolf. At the same time, he can look at rambunctious and charming Christopher Reimer with special satisfaction and join his parents in saying "Wow. We did it".

Christopher Reimer with
Dr. Marvin Fritzler

Achievements:

- Discovered effective diagnostic techniques
- Established an international diagnostic centre
- Improved patient care
- Discovered lupus is related to other health problems
- Educated physicians about the disease

Challenges:

- Use techniques to unmask causes of lupus
- Monitor effects of current therapies and develop new ones
- Coordinate multi-centre international research

Controlling Cholesterol

The word "cholesterol" strikes fear in the hearts of bacon and egg eaters. If not fear, at least a little guilt. Well it should, because a one percent increase in the level of blood cholesterol raises the risk of a heart attack by two percent.

Who's really in danger? It's estimated about a third of North Americans are, but they don't know it.

A new team of researchers at the U of A are tackling the problem from the source. They are investigating the molecular biology of the disease to find better ways of controlling it and hopefully preventing it, even in people whose genes predispose them to atherosclerosis.

The researchers have been recruited from Edmonton, Vancouver, Tucson, Nottingham, and Osaka—and each brings a different approach to the problem. They've formed one of the world's foremost study groups in the field.

"We understand how cholesterol is made, but we don't understand all the control mechanisms," explains Dr. Dennis Vance, head of the group. Cholesterol is a fatty substance called a lipid which is acquired in the food we eat and is also made by the liver. It's converted to several forms, travels to tissues and back to the liver via transport molecules called lipoproteins. This complex system means there are many potential points to intervene before excess low density lipoproteins (LDLs) collect and clog arteries.

"IT WAS A KILLER OF A PROBLEM," admits Dr. Vance, but he solved it, something others had tried to do for 20 years. He purified a key liver enzyme and subsequently showed that blocking the synthesis of a lipoprotein decreases the transport of harmful LDLs. This opens up new possibilities for controlling blood cholesterol levels.

IT'S THE CHICKEN OR THE EGG. Since eggs are cholesterol rich, it's not surprising hens have massive amounts of cholesterol. "Why don't they get atherosclerosis?" asks Dr. Wolfgang Schneider. It's because the hen has a very efficient system to deliver the cholesterol only to the egg yolk and not other cells. He's identified key cholesterol receptor proteins, an achievement that earned him six major national and international awards.

THE MARVELLOUS SPHINX moth is an eating machine in the larval stage so it can store up lipids for energy. Its preparation for adulthood when flying long hours in search of a mate is more important than eating. This makes the moth an excellent model for Dr. Robert Ryan's research on lipid transport and metabolism.

THE STRESS FACTOR is another approach. "It's commonly acknowledged there's a stress component to illness, but it's difficult to translate that into mechanisms in the body," says Dr. David Brindley. He is, however, doing exactly that. His research shows that the hormonal changes which accompany stress increase cholesterol levels in three ways. Diet or drugs can modify the process.

PATIENT CARE is Dr. Shinji Yokoyama's specialty, complemented by his basic studies on lipoprotein transport. He is an international authority on current and emerging drug therapy. He and Japanese colleagues have also pioneered a new therapy which, according to trials, can actually reverse early stages of atherosclerosis. The dangerous LDLs are removed from the bloodstream in a process called apheresis. It has saved the lives of people who are missing the gene for LDL receptors in the liver.

"The idea is simple, but the technology is complicated," says Dr. Yokoyama.

Achievements:

- Successful recruiting of scientists with complementary expertise on a single problem
- Progress by each group member has led to potential new approaches for controlling cholesterol levels
- A leading edge therapy is available to Albertans

Challenges:

- To provide enough funding to maintain the momentum of a talented group
- To take basic research forward through the consecutive stages to clinical studies

The U of A Lipid and Lipoprotein Group:
(left to right) Dr. David Brindley, Dr. Dennis Vance, Dr. Wolfgang Schneider, Dr. Robert Ryan and Dr. Shinji Yokoyama

> *"We're able to do things we couldn't do even two years ago."*
>
> Dr. Dennis Vance

The Globe and Mail
110 Soviets shuffled out of limelight

Electric Therapy for the Paralyzed

Three years ago Oscar Gilbertson was a young man on an adventurous holiday in Southeast Asia. He'd taken time off from his job as a metallurgical engineer for Syncrude to explore the world a little. One evening he was walking back to his hotel after a sociable evening in a Thai village when one of the locals he'd met offered him a ride. Oscar accepted. Minutes of terror later, the jeep was overturned and Oscar was on the ground unable to move any part of his body.

He was flown back home in a body cast and at first was told he'd never walk again. With surgery, physiotherapy, and incredible will power, Oscar gained back most of his function, except for a leg that doesn't work properly. Even with crutches Oscar walks slowly, with great difficulty and that's not Oscar's style.

"I'm lucky to be part of this, right here in Edmonton too. In the long run, it's going to help a lot of people who are even worse off than I am."

Oscar Gilbertson

Lately Oscar takes a faster pace, thanks to innovative electrical stimulation (ES) therapy pioneered by Dr. Arthur Prochazka and his colleagues at the U of A. The principle is similar to the one used in cardiac pacemakers. Carefully controlled electrical currents replace the natural small electrical currents which normally activate muscles.

The system works like this. U of A surgeon Dr. Lyle Davis implanted a fine wire electrode into Oscar's hip flexor muscle. The end of the wire is attached to a small box Oscar wears like a Walkman. The electric current comes from this box which is also connected to a sensor in Oscar's shoe on the good leg. Stepping on this leg triggers the electrical stimulus to activate the hip muscle which moves the weak leg forward.

The device allows Oscar to walk more smoothly and with less effort. Even though the ES system was well developed, adapting it for Oscar is a technical challenge because sometimes a tremor-like muscle movement of his weak leg sets off the stimulation at the wrong time. Working out the details doesn't bother Oscar. He has that indomitable willpower and as an engineer he knows new systems can take time. He says, "It takes patience. I know it's going to work. It was meant to be. And besides, I saw how it helped Joe."

Another of Dr. Prochazka's patients, Joe (not his real name) was the first stroke patient in Canada to be rehabilitated with ES applied with an implanted electrode in the hip. He was also the first such patient in the world to use the hip pacemaker system at home.

Scientists in Yugoslavia and Cleveland are also developing ES systems for paralyzed patients, but so far their systems have been bulky and impractical for home use.

Dr. Arthur Prochazka holds a control box

Help for Parkinson's and Spinal Cord Patients

Early in 1989, Dr. Prochazka and his team were the first to use ES to control tremors in a patient with Parkinson's disease and another with multiple sclerosis. In Oscar and the stroke patient, ES activates paralyzed muscles. In the tremor patients, ES suppresses unwanted muscle activity by stimulating the muscles which naturally act in opposition to those muscles causing the tremors.

"This is an exciting extension of what we've done before, an unexpected new application," says Dr. Prochazka. In the lab next door to Dr. Prochazka's, colleagues Dr. Richard Stein and Dr. Dejan Popovic are helping spinal cord patients walk with electrical stimulation applied through surface electrodes. Though at this stage ES therapy supplements wheelchairs rather than replaces them, it makes a big difference to paraplegics such as Blaine Pederson, a car accident victim. "Getting up out of the wheelchair and walking is such a great feeling," he says.

All three scientists are confident ES therapy will become widely used in the future, as electronic technology advances rapidly. (Consider that 30 years ago, the first cardiac pacemaker patient trundled equipment around in a huge cart.) "Functional electrical stimulation will become commonplace rather than the exception—it's just a matter of time," predicts Dr. Prochazka.

Achievements:

- Neurosciences Rehabilitation Group established in Alberta by capitalizing on local talent and recruiting others from London, England and Yugoslavia.
- Scientists have pioneered therapy for stroke, spinal-cord and tremor patients
- Program integrates engineering innovations and medical expertise, basic and clinical research

Challenges:

- To improve the technology and to apply it to more patient problems
- To provide adequate funding for larger clinical trials when appropriate
- Where applicable, to develop (or have others develop) innovative technology for commercial purposes

Dr. Wanda Wenman

Stalking the Silent One

The dreaded AIDS is not the most common venereal disease. Nor is herpes or gonorrhea. Far more people have chlamydia—one million Canadians and 500 million world-wide are infected. It's called the silent venereal disease because sometimes there are no symptoms: you can have it and not know it.

Though it's easily cured by antibiotics, it often goes undetected until after damage is done. In women, chlamydia causes pelvic inflammatory infection which is the leading infectious cause of infertility. Babies born to women with chlamydia are at risk for eye infections and pneumonia. Some African studies suggest this venereal disease is a risk factor for AIDS.

Dr. Wanda Wenman is tackling *Chlamydia trachomatis* with the tools of molecular biology. Because the organism is difficult to grow in culture, very little is known about it. As a young pediatrician newly graduated from the U of C, Dr. Wenman decided to do something about that.

Her research on how the organism causes infection has provided tools useful for improved diagnosis, the first step in treating the disease. Most important, she has discovered new opportunities for prevention through a vaccine.

Finding a Vaccine

Dr. Wenman has identified two proteins in the organism which attach it to the host cell. These two proteins are candidates for a vaccine. Because of this work, Dr. Wenman was courted by several multinational firms vying to be her partner in developing the vaccine. She chose to sign a partnership agreement with one of the world's leading vaccine production firms, Institut Merieux of France. Under the agreement the University of Alberta receives a share of any royalties and the firm provides generous research funds, a portion of which goes to the University.

Wanda Wenman wears two hats. Wanda Wenman, the medical researcher investigates the molecular biology of chlamydia and another disease, beaver fever. Dr. Wenman, the pediatrician specializes in infectious diseases of childhood at the U of A Hospital. Because she is Northern Alberta's only pediatric specialist in the field, there are fierce demands on her time.

"I spend most of my day on the phone talking to physicians in and around Edmonton and seeing patients." She helps physicians with the difficult cases—perhaps a child with persistent pneumonia, a fever with no apparent cause, or a bone infection which isn't healing. "I'm available virtually every day and every weekend of the year and it's exhausting," Dr. Wenman admits.

Then why does she struggle to maintain her research program? "I enjoy the creativity of research—designing an experiment and then finding ways to make it work better, faster."

There's the creative satisfaction and there's the pressure. On one hand, sick children out there need Dr. Wenman's expertise and on the other hand there's the knowledge that, for every day she doesn't spend in the lab, she's losing the competitive edge internationally and the opportunity to finally win out over the organism. It isn't easy and that's one of the many reasons Wanda Wenman is special.

The Art of Seeing

Ever since he was a small child in Ontario, Robert Berdan has been fascinated by the intricate beauty of the world and determined to find out how things work. In grade six he spent hours with a toy microscope. In grade eight he saved up to buy a research-quality microscope. In high school he persuaded university professors to give him some culture medium for his homemade "light bulb" incubator in his lab in the family garage.

His fanatical enthusiasm has only increased with time. When choosing a medical research area he went for the most complex—the brain—to explore some of medicine's most intriguing questions. "What makes us sleep? What's memory? Why do we age? I've always been fascinated with the brain and physiological questions that border philosophy," says Dr. Berdan.

He's found a way to study some of the fundamentals of underlying brain activity and has spent the last ten years acquiring sophisticated techniques to do it. Dr. Berdan examines electrical synapses during development and nerve regeneration. These synapses are channels which allow small molecules or electrical signals to pass between nerve cells so they can communicate. "We know electrical synapses are very important during development, that they diminish after that and reappear in old age, but we don't know their purpose," he explains.

While an AHFMR Fellow in Dr. Andy Bulloch's lab, Dr. Berdan developed a snail model which he speaks of with the same enthusiasm other people reserve for their pets, their cars or their private businesses. Because the large neurons of snails are well mapped, he can trace what happens when he blocks activity of electrical synapses with chemicals. He works with live animals and cell cultures, never losing his sense of wonder, as he watches a damaged snail neuron regenerate, sometimes within hours.

Yet for Dr. Berdan, the intellectual and aesthetic appeal of studying snail cells is not the end point, though he admits it is for some researchers. The point is that the simple snail system is used to answer questions about the human body. He explains that others have found electrical synapses may play a role in cancer where cell growth goes wild, in epilepsy, and in blindness of premature babies who are placed in oxygen chambers.

Dr. Berdan's sense of wonder has led him to electron microscope photography, a passionate avocation which has earned him awards. For him, the art of seeing is an integral part of the art of science.

"I wanted to do research because I found a lot of things fascinating, and to me there just isn't anything you can do that is more challenging. It combines not only a thirst for knowledge but the fact that things are beautiful. Art and science are almost one—Da Vinci did art and science and I think the two are closely related. To be a good photographer you have to be observant. You have to be able to see things and isolate them amongst the 'noise'. Scientists have to do the same thing. We've got to notice something that somebody else hasn't seen."

Dr. Robert Berdan

Dr. Cy Frank

Not Your Ordinary Doc

Cy Frank is not your ordinary doc. For a start, he's an arthroscopic knee surgeon who treats noisy knees, arthritic knees, athlete's knees, old knees, any difficult knees other physicians don't know how to heal. In the lab he invents tools, plays around with physics, and crumbles dogmas, all in the quest for ways to heal ligaments. Presently there are few proven non-invasive treatments for ligaments, but that doesn't stop Dr. Frank.

He chose his challenging path early as a young medical graduate from The University of Calgary. "One of the things I've learned is that too many people accept dogma and simply apply existing tools to problems. We need to believe there are other possibilities. If we can put a man on the moon, we can heal ligaments.

"When I graduated in orthopedic surgery I reached the great fork in the road—whether to pursue these things and try to solve problems or simply apply technology to the clinical setting. It didn't take me long—about one second—to decide the excitement is in answering questions. I knew it could be done and I started believing maybe it could be me. The Heritage Foundation was the major pathway to fulfilling these dreams (A post-graduate Fellowship to study abroad and then a Scholar position) ...and now I want to create a similar environment for others in orthopedics and surgery to do the same thing, again made possible by the Heritage Foundation and partly by other granting agencies."

Dr. Frank has found that electrical stimulation and magnetic fields can heal ligaments or harm them depending on circumstances. He works with both animals and tissue cultures. Fascinated with how electricity and magnetism can affect tissues, he's pursuing the mechanics behind it in cooperation with medical colleagues, engineers and computing scientists at the U of C. He and his colleagues have a grant from an American medical technology company to apply its electrical stimulation system for bone healing to ligament healing and another grant from a Canadian firm to further develop electronic research techniques.

These electromagnetic studies are one area where physics enters the picture. "Physics for 21st century biologists is a major development that's going to occur, for example in understanding communication between cells. I think there are some fundamental breakthroughs as big as anything that has ever been discovered, as big as DNA, bigger. That's going to sound very weird coming from an orthopedic surgeon," he laughs.

Cy Frank, the inventor, and engineer Nigel Shrive have devised several innovative tools such as a device for arthroscopic surgery, but Dr. Frank is most excited about a tool which measures forces on tissues in animals—physics again. "There's an interaction of forms of energy on tissues and once we can measure them, I think we'll find it's one of the big secrets of how to control behavior in normal or healing tissue. I think we're onto something big."

Researchers in other countries are clamouring to use the team's technique for quantifying collagen and remodelling in scars. Never possible before, this has been a goal of scientists for decades and it's applicable to many healing situations, not just ligaments.

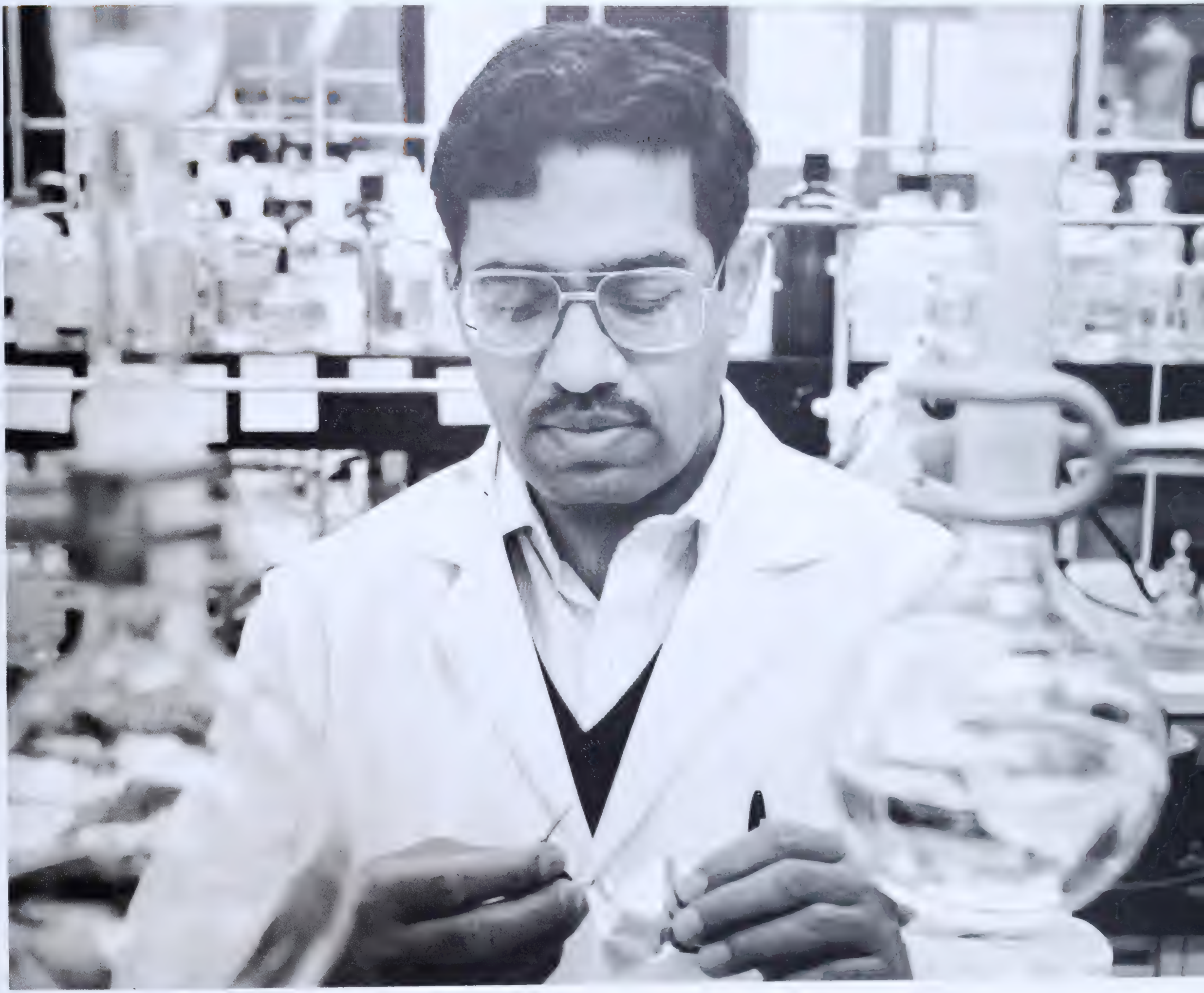
Ligament transplantation studies offer new hope for athletes who have given up sports because of ligament injuries. While some transplants are now done in the U.S., it's generally a trial and error system. Dr. Frank and his colleagues are identifying the potential and the problems in animal studies, so that transplantation can be based on sound knowledge about ligament healing.

Dr. Frank's Joint Injury and Disease Research Group has about 25 people including six researchers, their collaborators, fellows, students and technicians. Together they conduct more than 30 studies ranging from musical knees (noisy knee joints may forecast osteoarthritis in old age) to anti-inflammatory drugs. A community health survey they did through the Foothills Hospital Emergency department indicates present data on ligament injury is probably conservative. Each year one out of ten active people injure a ligament.

Healing those patients keeps Dr. Frank motivated. "It keeps my research relevant and reinforces the need to do it. The clinical work is fun and rewarding because I can see the results daily. It's rewarding to perform a ligament reconstruction on someone crippled and unable to do what they love to do." People like 19 year old Heidi Geier, a competitive gymnast. A ligament injury threatened to end Heidi's career until Dr. Frank reconstructed her knee. Now she's competing in the U.S. on a gymnastic scholarship.

As Research and Clinical Director of the U of C Sport Medicine Centre Dr. Frank has additional opportunities to combine clinical and basic research.

Dr. Frank talks about building the new research group housed in the Heritage Medical Research Building. "I want to spread the dream that the tools are there and it can be done. If we have an idea we can make it happen.... Some people would say 'In Canada? In Calgary? Give me a break!' But it can happen here just as well as at Harvard or the Max Planck Institute."



Dr. Bhagirath Singh

Serendipity has led to new hope for a **VACCINE FOR JUVENILE DIABETES.** Dr. Bhagirath Singh has discovered a vaccination protocol which blocks the development of juvenile diabetes in a diabetic strain of mice.

Diabetes is an autoimmune disease in which the immune system mistakenly sees the body's own pancreatic islet cells as foreign and therefore destroys them. Dr. Singh immunized mice with various proteins to see if he could prevent T-cells from setting off this autoimmune response. He gave the control group of mice only the adjuvant. Adjuvants are compounds routinely added to vaccine proteins. Dr. Singh used the same adjuvant Dr. Jonas Salk used for the polio vaccine in 1953. It turned out the control mice did not develop juvenile diabetes after 16 months, though they normally die of it at four months.

"It was a shock. But now we've confirmed it," says Dr. Singh. With the adjuvant, apparently the T-cells no longer react negatively to chemical signals from healthy tissue.

The discovery is not only exciting for diabetes research: it can also be applied to other autoimmune diseases such as lupus and rheumatoid arthritis. If serendipity comes to the deserved, then Dr. Singh was in line, for he is known for his productive research on T-cell immune responses.

If Dr. Timothy Lee can find a vaccine against the intestinal parasite which causes **ASCARIS** infection he will contribute greatly to world health. Though Canadians sometimes get *Ascaris*, it's a scourge in underdeveloped countries, affecting about a quarter of the world's population. Dr. Lee has studied how some hosts (pigs) reject the parasites and identified some antigens which are promising vaccine candidates. These immune studies are relevant to other inflammatory diseases such as Crohn's disease and asthma. A vaccine for *Ascaris* would also save the hog industry millions of dollars because pigs would not need to be routinely treated for *Ascaris*.

Few diseases have caused as much suffering to so many as **MALARIA.** Dr. May Ho is investigating the immune response to the mosquito which causes the most serious form of malaria in an effort to develop a more effective vaccine and more effective drugs. A University of Calgary researcher, she conducts part of her studies at Mahidol University in Bangkok, Thailand. She is also a valuable resource to Calgary colleagues working on infectious diseases.

Another parasitologist, Dr. Dean Befus, studies host defence mechanisms against *Giardia*, the parasite which causes **BEAVER FEVER**. This lays the groundwork for vaccine development. This and other studies earned him the 1988 Henry Baldwin Award from the American Society of Parasitologists.

Dr. Wanda Wenman has identified two vaccine candidates for the most common **VENEREAL DISEASE**, chlamydia. (See p. 15)

The recent **MENINGITIS SCARE** in Ontario shows that epidemics can still occur in Canada. Elsewhere in the world it is a chronic problem. Dr. Anthony Schryvers' original studies on two of the organisms which cause meningitis show how they acquire iron from human hosts. Since the organisms need iron to survive, this information is a big step towards developing a more effective vaccine which will protect infants. Present vaccines do not.

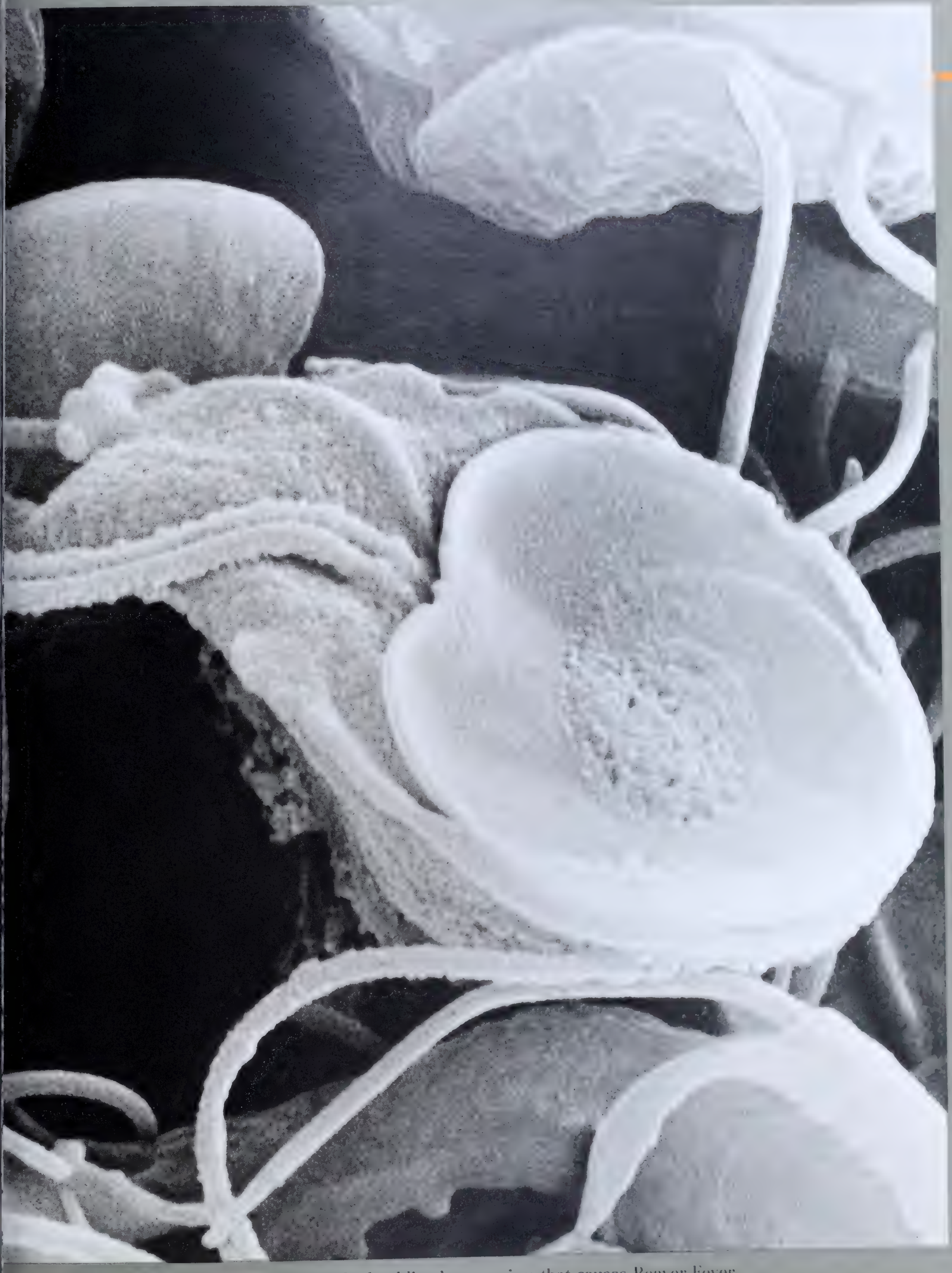
The **PERTUSSIS CONTROVERSY** is settling as recent research shows the current vaccine for whooping cough does not cause neurological damage, though it can have temporary side effects. Dr. Mark Peppler and an American collaborator have used genetic engineering to develop a modified, less toxic vaccine which is ready for testing in animals.

Achievements:

- More information on immune response to diseases has allowed scientists to develop new vaccines
- AHFMR scientists are also using DNA technology to improve existing vaccines

Challenges:

- To discover more immunological information and apply it to vaccine development
- To advance vaccine studies to the clinical stage



An electron micrograph of *Giardia lamblia*, the organism that causes Beaver Fever

Dr. Cathy Lord with Eric Shirley

YES HE CAN. Eric is coming out of the enclosed world of autism where the simplest everyday communication—a greeting, a smile, a conversation— often doesn't occur. Eric is learning how to relate to people and find a place in the world.

Psychologist Dr. Cathy Lord has helped to open the door for Eric. She runs special therapy groups where autistic young people can learn social skills formerly considered impossible for them.

Dr. Lord's research and her personal commitment keep her from accepting conventional limitations. Her comprehensive descriptive studies show that autistic children actually do smile and do try for eye contact, but not when another person is smiling or looking at them. These and other findings have changed the diagnostic criteria for autism and have led to her new therapeutic approaches.

"You have to have reasonable expectations and be happy with small changes, but they do happen and that's very rewarding," says Dr. Lord. "What's most rewarding is seeing some children come to feel happy and secure in themselves and find their place in the world."

With four research groups in England and the U.S., she is also conducting one of the most comprehensive studies of autism, a very poorly understood disease. She examines genetic factors which probably account for at least some autism. She also looks at neurological factors and is separating retardation from autistic behaviour, a difficult distinction.

ONE IN THREE PEOPLE suffers from a psychiatric disorder during a lifetime. Dr. Stephen Newman is helping identify mental health problems in one of the first thorough Canadian epidemiological analyses of how mortality risk relates to psychiatric disorders in a given population, (Alberta).

A VIRUS MAY BE THE CULPRIT IN MS. Dr. Aimo Salmi has evidence multiple sclerosis may involve contracting a viral infection years before the disease appears. He also has new information about how the disease affects the immune system.

CRIB DEATH IS A COMPLETE MYSTERY but Dr. James Fewell has detected a promising clue by studying breathing and sleep in normal infants and animals. His work indicates the problem in crib death may be a faulty arousal response when breathing is blocked for a few seconds.

IT'S NOT ALWAYS MOTHERS' AGE which causes chromosomal abnormalities leading to retardation and other birth defects. Dr. Renée Martin is the first to identify chromosomal abnormalities in sperm and relate them to high risk factors such as fathers' age and radiation exposure.

NOBODY KNOWS WHY SEIZURES OCCUR but Dr. Brian MacVicar may have at least part of the answer because he has discovered a new role for cells in the brain called glial cells. His studies suggest oscillation of glial cells could initiate seizures.

FOOD ALLERGIES have never been explained. Dr. Joe Davison's study of how nerves control gastrointestinal (GI) function and Dr. Brent Scott's work on GI motor activity indicate some of the possible underlying factors in allergies.

About 50,000 Albertans suffer from **PSORIASIS** in varying degrees. There is no known cause or cure, though heredity is involved and perhaps a virus. Dr. Tony Garber is exploring both avenues in his molecular studies of the disease, the first of their kind.

Achievements:

- AHFMR has successfully recruited researchers with specialized and often unique expertise who bring new approaches to old problems
- Progress by individual scientists is extensive and taken as a whole, the variety of studies represent a balanced program of research

Challenges:

- To maintain a grant system which gives scientists the time and freedom they require to follow up on the clues to mystery diseases
- To adequately support creative scientists with novel approaches to problems
- To recruit colleagues with complementary expertise as the need arises

The Technological Edge

"I MAKE MOVIES the way Spielberg does," laughs Dr. Frank Witkowski. His movies follow electrical activity in a single heart beat at hundreds of sites simultaneously. The information is allowing him to learn why therapy called defibrillation saves the lives of some heart attack patients and not others.

In defibrillation the heart is given a massive electrical shock to restore electrical activity that's gone wild, making the heart beat too fast and irregularly. Nobody knows exactly why defibrillation works or doesn't work because the question requires extremely complex technology that didn't exist.

That hasn't stopped Dr. Witkowski, a cardiac physician and former professional engineer. He's spent two years designing and building one of the world's largest cardiac mapping systems which takes heart muscle recordings from 384 sites. He's also developed and patented miniature low noise electrodes which allow him to see what happens in the process of defibrillation, information that's never been available before. The electrodes

Dr. Frank Witkowski

already have spin-off uses in cardiac surgery, but Dr. Witkowski expects their most important use will be aiding the development of better implantable defibrillators. These devices have already proven valuable, but they are still too bulky and too expensive to have the same broad clinical application as pacemakers.

"We've made a lot of progress," he says, "but there's more to do and the harder it is, the more challenging and the more fun it is."

This image is a **WINDOW IN THE BODY** created by magnetic resonance technology. Unlike X-rays or CAT scans which only show structure, MR technology also allows researchers to assess tissue function. For example, they can track how a tumor grows or responds to therapy. Dr. Peter Allen heads a $4.5 million MR research program at the U of A. A team of researchers works on MR studies of cancer and other diseases. By special arrangement, the state-of-the-art MR equipment financed by AHFMR is also used by physicians for patient care.

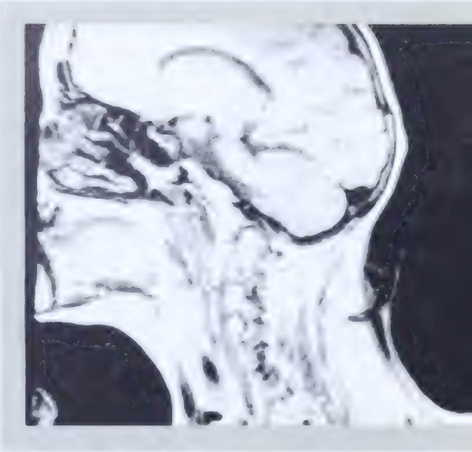
THE INGENIOUS METHODS OF BIOTECHNOLOGY allow scientists to produce medically important proteins not otherwise available in large enough amounts for research or therapy. Dr. Sui-Lam Wong is developing a new biotechnology system using the bacterium *Bacillus subtilis* as a factory. He's used the system to successfully produce a clot-dissolving drug.

CAN THE BABY HEAR? Dr. Jos Eggermont may be able to answer that question better than anyone in the world. He has pioneered the use of electrodes to measure hearing in the inner ear and has refined techniques to measure auditory activity in the brain stem. His superior diagnostic techniques are now available to physicians at the Alberta Children's Hospital where he helps them assess hearing in premature babies. He also collaborates with physicians who use his expertise to determine why cochlear implants work for some adults, but not others.

Dr. Eggermont's basic research on frogs includes exciting evidence that hearing development may be more dependent on the environment than was thought. This opens up possibilities for new therapies.

Dr. Robert Campenot's compartmentalized culture system to study **NERVE CELL REGENERATION** has been adopted by researchers throughout the world. For example, a multinational pharmaceutical firm uses it to screen drugs for Alzheimer's disease.

Innovative research often demands customized tools that don't exist. Dr. Jonathan Tyler, Director of the **BIOMEDICAL DESIGN FACILITY** at the University of Alberta designs such tools. For example, he has designed a specialized magnetic resonance probe for studying muscle proteins and viruses.



A magnetic resonance image of a head and neck

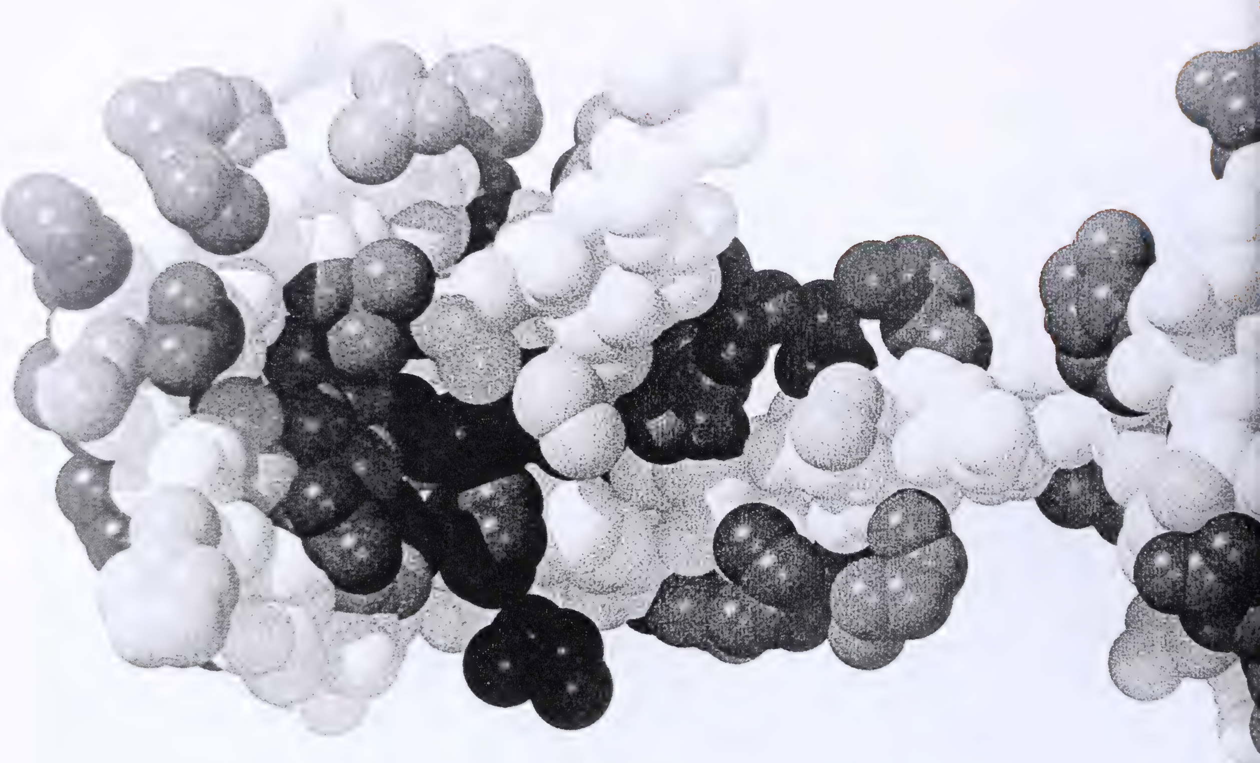
Achievements:

- AHFMR scientists have developed superior methods to diagnose: eye movement problems from stroke or tumors, autism, lupus, inherited metabolic diseases, heart diseases, urinary problems in the elderly, risk for diabetes, advancing breast cancer, food poisoning, venereal disease, and others
- They have developed novel research techniques to study: drug action in the CNS, natural brain chemicals, ion channels, glucose tolerance, intestinal function, muscle cells in disease, and many others
- The exceptional equipment support from AHFMR—in some cases the reason prestigious scientists came to Alberta—has given researchers a competitive edge

Challenges:

- To keep the technological edge in fiercely competitive fields
- To give new scientists the same opportunities
- To capitalize on innovative research techniques
- To develop more techniques for tasks that are now impossible but are essential to understanding the causes of disease

Pills and Potions



This is a 3-D computer-generated model of a protein molecule in the body. Created in a sophisticated process called **X-RAY CRYSTALLOGRAPHY**, models like this allow researchers to simulate interactions between drugs and target molecules, interactions which take only milliseconds in the body. By analyzing the structure of the target, researchers can take the chance out of drug discovery. They can design drugs that will exactly fit the target molecule like a lock and key. This means the drug is likely to be more effective and certainly will have fewer side effects than drugs found by trial and error screening.

Crystallographer Dr. Penny Codding, has identified the site where valium binds to its target molecule and she's using this information to design improved antidepressants. She's also working on new epileptic drugs. Dr. Randy Read uses x-ray crystallography to identify a drug for African sleeping sickness and to further develop the technique for designing other drugs.

Dr. Michael James' crystallography studies have led to a breakthrough in the search for a better hypertension drug. He's identified the binding site of renin, an enzyme key in the development of high blood pressure.

Achievements:

- New drug therapies have been identified and tested for diseases such as cardiac disease, allergies, lupus, arthritis
- 30 AHFMR researchers have identified the mechanisms of action in drugs for diseases such as epilepsy, depression, hypertension, stroke
- 28 researchers have identified receptor molecules for proteins or enzymes, information which could lead to new drugs for diseases ranging from coronary artery disease to epilepsy
- 21 researchers are collaborating with multinational pharmaceutical companies because the companies need the scientists' basic research expertise

Challenges:

- To take drug development through the many stages to clinical use
- To maintain or increase support for basic research related to rational drug design

A 3-D computer-generated image of troponin C, a protein involved in muscle contraction

Dr. Susan Jensen and two colleagues have developed a technique for producing **MORE POTENT AND CHEAPER ANTIBIOTICS.** Most new antibiotics are created by chemically altering natural antibiotics such as penicillin. This can take months, years or even decades. Production with the new cell free enzyme system is much faster. For example, an antibiotic that takes six months to make conventionally, can be made in two days with the new technology.

OUTSMARTING CLEVER BACTERIA that have learned how to develop resistance to antibiotics isn't easy. Dr. Diane Taylor is making progress in her studies of a bacterium which causes common infections such as blood poisoning.

Dr. Roland Auer's animal studies indicate that a combination of insulin and a drug called MK-801 given soon **AFTER A STROKE** reduced the amount of permanent brain damage.

Though they don't know it, some heart attack patients are alive, thanks to Dr. Henry Duff's research. He has discovered new drug treatments for **HEART ATTACK** patients whose arrhythmias (see p. 6) did not respond to known treatments. Amiloride, sotalol and melperone all suppress the dangerous heart rhythms. He's found other patients respond best to a combination of drugs. Dr. Duff's many achievements stem from a solid basic research program where he studies how cardiac drugs affect electrical activity in heart cells. In clinical work, he has also shown that a drug monitoring service for physicians saves money and improves patient care.

HIGH BLOOD PRESSURE is such a widespread problem researchers around the world race to find the most effective drug to control it. Because blood vessels are lined with smooth muscle, Dr. Michael Walsh's studies of how proteins control smooth muscle contraction provide valuable information for designing drugs. He collaborates with two Swedish pharmaceutical firms and has acted as a consultant for four others.

ANCIENT WISDOM MEETS HIGH TECH in the Traditional Chinese Medicine Program at the U of A. Dr. Peter Pang and Dr. Larry Wang lead a joint Chinese-Canadian study of Chinese herbal medicine. Herbs such as those used to treat high blood pressure have been used successfully for centuries in China. Some herbs have moved from folk medicine into modern institutional medical care in China. While one Chinese person drinks medicinal herbal tea as his ancestors have done for 3,000 years, another may be taking in the same herb through an IV in the nearest hospital. With the new program, antihypertensive herbs and others may someday be available to Canadians. The Alberta researchers are applying sophisticated pharmacological research techniques to understand how the herbs work and establish their scientific credibility according to Western scientific standards. Because the herbs are natural, they have fewer side effects than current drugs for hypertension.

First Causes

IS CANCER INHERITED? Yes and no, according to Dr. Malcolm Paterson who heads a $2 million dollar research program on the genetics of cancer at the Cross Cancer Institute. While we do not inherit cancer, apparently we can inherit a susceptibility to it. Cancer is caused by many interacting factors, inherited and environmental.

Dr. Paterson studies cancer-prone families and individuals with inherited diseases which make them exceptionally susceptible to cancer. He has found that some people lack an enzyme required for DNA repair from carcinogens such as sunlight.

"Our cancer risk is a product of what we do and who we are," he explains.

Dr. Paterson's other studies on the genetics of cancer have led to an important clinical tool. He has found that a recently identified cancer-risk gene can be used as a diagnostic marker to determine which women with early stage breast cancer are at risk for a relapse after surgery and therefore require other aggressive therapy. There is presently no way to determine this.

Dr. Malcolm Paterson

If researchers could understand **HOW VIRUSES HOOK** on to cells, they could look for new ways to stop the attachment. Dr. Patrick Lee has identified the binding site for reoviruses on human red blood cells. Dr. Jerry Wang leads a $4.5 million group which investigates cell activity so fundamental that findings could be applicable to almost any disease imaginable. The Cell Regulation Group generally studies how healthy cells adapt to environmental changes and how they receive signals to do their jobs. For example, one study looks at how calcium concentration is controlled in cardiac cells so that they can pump the heart. Several group members collaborate with drug companies who need such fundamental data to design new drugs.

THIS DELIGHTFUL LITTLE WORM is yielding secrets about what happens in the beginning of life. Dr. James McGhee wants to know how particular genes get turned on only in certain cells of a developing embryo. He calls *C. elegans* an elegant creature, ideal for study because the adult has only 1,000 cells (compared to trillions in the human) and the cell lines of development are known. He's followed the paths taken by the actual DNA molecules contributed by father worm's sperm and mother worm's egg during embryonic development. "Rather remarkably, the DNA segregation turns out to be completely random," he says.

101 WAYS TO TRANSFORM A CELL or the root causes of cancer are explored by these researchers and many others. Dr. Grant McFadden has developed an animal model of a tumor-promoting virus. Dr. Linda Reha-Krantz investigates the biochemical basis of mutation by examining an enzyme critical to DNA replication. Dr. Roseline Godbout studies chick retinas to understand gene control during early cell differentiation and hopefully gain understanding about the causes of retinal cancer and blindness.

Dr. Donald Fujita has identified 25 new mutants of the human c-src proto-oncogene. All the mutants have lesions that transform healthy cells into cancerous ones in culture or animals.

VIRUSES AGAIN. This time the connection is diabetes. Dr. Ji-Won Yoon has shown that two different viruses are associated with juvenile diabetes. He's also identified differences between diabetic and nondiabetic viral genes in animals.

Dr. Henry Koopmans believes **OBESITY IS MOSTLY PHYSIOLOGICAL**, not psychological. His evidence from animal studies suggests that neuronal or hormonal signals control food intake in the gut.

BREATHING EASY is impossible with asthma and other severe lung diseases. Dr. Dale Lien's studies on the role of white blood cells called neutrophils are revealing new clues about why these diseases occur.

Achievements:

- Because understanding the genesis of diseases at the molecular level is our best hope for effective cures and for prevention, AHFMR has established an extensive and very sound program of basic research in immunology, genetics, virology, bacteriology, cardiology, and other areas
- AHFMR scientists are using the most advanced technology to discover basic mechanisms underlying various diseases

Challenges:

- To continue recruiting quality scientists whose work has potential for broad application
- To continue integrating basic findings with animal and clinical research and vice versa
- To develop new treatments and preventive measures based on better understanding of how healthy bodies remain healthy and knowledge about how diseases begin

Dr. Pamela Sokol and Dr. Donald Woods

Leading the Way in Canada and Abroad

U of C researchers have a plan for **KEEPING CF PATIENTS OUT OF THE HOSPITAL.** These patients have a powerful and sometimes fatal enemy called *Pseudomonas aeruginosa*. This tiny bacterium causes a lung infection in most CF patients.

Studies by U of C researchers offer new hope for managing the disease. Dr. Donald Woods and his colleagues are looking for ways to genetically regulate the toxins that the bacterium produces. In 1988 the Cystic Fibrosis Foundation contributed $1.5 million to establish the Canadian centre for CF lung research at the U of C. Calgary was chosen because there was a critical mass of scientists with varied expertise and because they take a molecular biology approach to understanding how the bacterium causes infection.

The group has initiated a new therapy for CF patients which is expected to keep them out of the hospital for *Pseudomonas* infection. Presently, when it becomes severe, patients are hospitalized for about two weeks and given antibiotics to which the bacterium often becomes resistant. In the U of C trials, patients are alternately given two proven drugs continuously so that there is no opportunity for resistance to develop towards either drug. The trials are based on years of basic and animal research by the group. Patients are primarily from Calgary, but include some from Vancouver and Saskatoon.

"This is everything one hopes for as a researcher," says Dr. Donald Woods, head of the group. He and his wife, Pamela Sokol, another AHFMR scientist, moved to Alberta seven years ago because AHFMR was committed to long-term funding and multidisciplinary research. "It's a tremendous opportunity to work with people in many different fields who are interested in the same problem and bring all their resources to it. Basic lab studies, animal research, and clinical trials: we can do all these at once."

The work goes beyond Canada's borders. For example, Dr. Woods collaborates with researchers in Switzerland, Denmark, West Germany and eight American universities.

Dr. Neil Finer and his colleagues may have a way to reduce **BRAIN DAMAGE IN NEWBORNS** who have insufficient oxygen at birth. Dr. Finer has organized a study in ten Canadian cities to see if prophylactic phenobarbital will prevent seizures in these infants. Currently the drug is given after seizures begin; but animal studies indicate, if it's given before seizures occur, they are reduced. This is probably because the drug increases oxygen to the brain.

Dr. Leigh Field's **GENE MAPPING** expertise has been important to an international multi-centre study on the genetics of insulin-dependent diabetes. She is the first in the world to show that a predisposition to diabetes involves an interaction of genes on two different chromosomes. She helps other Alberta researchers track diseases such as manic-depression and Crohn's disease.

The Calgary cardiac group's participation in the international CAST trial has further established their reputation as one of the leading arrhythmia labs in the world. (See p. 6)

OCCUPATIONAL LUNG DISEASE has been one of the Cinderellas in medicine. Dr. Francis Green's rare expertise in analyzing lung damage from mineral and organic dusts is in demand internationally. Researchers in China, Wales, and the U.S. have asked for assistance in studying miners' health. In Alberta Dr. Green has advanced knowledge about sour gas damage to lungs. He has also assessed the risk of LUNG DISEASE AMONG FARMERS who constantly are exposed to soil and grain dust.

Because Dr. Grant McFadden has established an important animal model to study **VIRUSES WHICH INDUCE TUMORS,** other leaders in the field are anxious to work with him. He's Chairperson of a National Institutes of Health (U.S.) special study section and his collaborations include studies at prestigious centres such as Harvard Medical School, Dana Farber Cancer Centre, Rockefeller University, Cornell Medical School, and a hospital in Cambridge, England.

Achievements:

- AHFMR researchers are part of a national and international network of leaders
- 82 AHFMR scientists have international collaborations
- Some AHFMR researchers are initiating national and international studies
- Since 1980 AHFMR has supported 147 national and international conferences to promote the network and make others aware of activity in Alberta.
- AHFMR has supported a total of 85 visiting scientists to and from Alberta

Challenges:

- To build upon the networks established
- To use emerging AHFMR international leaders to recruit more quality scientists
- To provide a level of funding which allows researchers to maintain the international contacts necessary to keep them on the leading edge of what's happening anywhere in the world

From Lab to Marketplace

"It changed my whole life," says the patient, Mr. Nasie Schnell.

"It's satisfying to know the therapy is so effective and we've put the patient out of danger," says the researcher, Dr. John Remmers.

"When it hit the market the response was phenomenal," says the company's marketing manager, Mr. George Cavagnaro.

They're all talking about Tranquility, a device to treat victims of sleep apnea or **THE SNORING DISEASE.** The story of Tranquility is a model of technology transfer where innovations emerging from research are transferred to industry and then patient care.

Though snoring is a major symptom, sleep apnea is no joke. It's a debilitating and sometimes fatal condition affecting about three percent of the population. Caused by a blockage in the upper airway, sufferers momentarily stop breathing while asleep, not once but hundreds of times during the night. Lack of oxygen and daytime sleepiness can have disastrous physical and social consequences. Though surgery sometimes helps, there is no cure for the disease. However, apnea can be controlled with a sleeping mask hooked to a machine which pumps air into the nostrils.

Dr. John Remmers, a world authority on the disease, founded The University of Calgary Sleep Clinic where patients are diagnosed and treated. Based on years of basic research and

Mr. Nasie Schnell

Dr. John Remmers holds the device for sleep apnea patients work with patients, Dr. Remmers devised a sleep apnea device superior to any on the market. It's more compact, quieter, easier to use, and provides more pressure for patients who need it.

Once Dr. Remmers had designed and initially tested the device, he and the U of C signed a development and marketing agreement with Healthdyne Corporation, an Atlanta-based firm specializing in home respiratory care. Healthdyne was delighted to work with Dr. Remmers because they knew he had a superior product.

Patients like Mr. Schnell had helped design it as they tried out the various prototypes. Dr. Remmers was equally delighted to work with Healthdyne because the company has experienced engineers and a dynamic executive committed to moving quickly and challenging the major competitor.

Though seven sleep apnea devices came out on the market in 1988, Tranquility took over an impressive market share from the company that had dominated it. The U of C was pleased with the shared royalty agreement and Dr. Remmers saw his innovation made available to patients who need help. He continues to work with Healthdyne in adapting the technology for a home device useful in other serious and even more common respiratory illnesses.

Though he admits at first he wasn't sure he'd wear it, Mr. Schnell enthuses, "It's fantastic. I wouldn't go anywhere without this equipment."

A new **ALBERTA MEDICAL INNOVATIONS PROGRAM** greatly expands the technology transfer activity of AHFMR. Announced by the Alberta Department of Technology, Research and Telecommunications in February 1989, the program provides another $9.3 million for commercialization of innovations. The funds originated from federal payments to the province under the amended Patent Act provisions.

Aurora Laser Inc. was founded on Dr. John Tulip's innovative designs for **MEDICAL LASERS.** One laser is ideal for endoscopic surgery and another is more portable than existing models for general hospital use.

Synthetic Peptides Inc. (SPI) was founded on the **PEPTIDE** expertise of Dr. Bob Hodges and Dr. Robert Parker. Because peptides are natural proteins which control many body functions, synthetic peptides are the basis for many new drugs. The company is presently developing a new drug based on an existing peptide hormone which is now used for a different purpose. The world market for the single product is estimated to be $300 million.

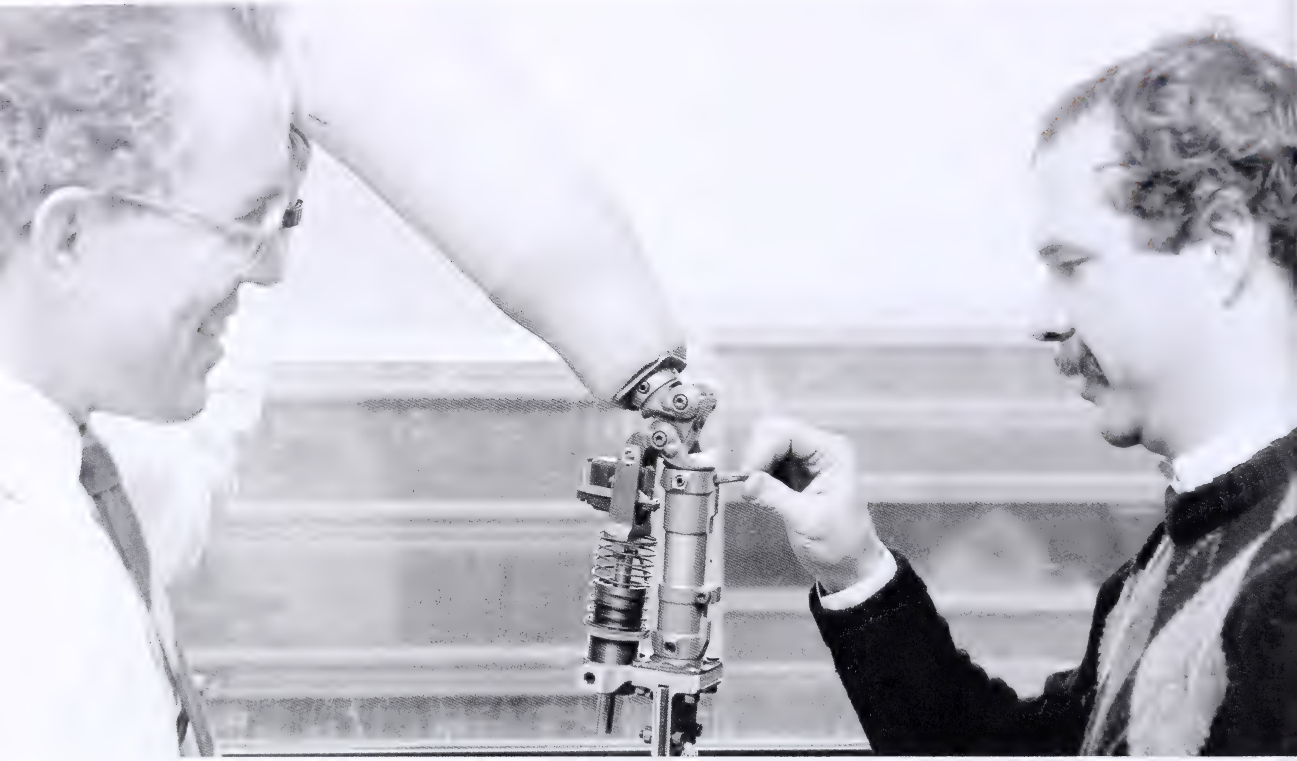
AMPUTEES HAVE MORE FREEDOM with two innovative prostheses. Dr. Richard Stein and engineer Mr. Kelvin James have designed a robotic knee in a superior artificial leg. The knee allows amputees to walk more naturally on all kinds of terrain, even stairs. Staff at Park Prosthetic Ltd., have devised the Alberta Ankle which allows amputees to change from barefoot to dancing shoe or ski boot in seconds. Both prostheses could be manufactured in Alberta.

Achievements:

- New health care products, new tools and patentable techniques are emerging from AHFMR labs
- Projects funded by the AHFMR Technology Transfer Program have formed the bases of a few new companies, have led to some products being patented and marketed, and have advanced work on other projects
- 31 scientists collaborate with commercial companies in fields such as: drug development, diagnostic tools, research tools

Challenges:

- To continue adequately funding the transfer of innovations to the marketplace and then to patient care facilities
- To keep commercialization activity in Alberta whenever possible
- To continue recruiting and funding creative scientists who generate innovations



Dr. Richard Stein and Mr. Kelvin James with the robotic knee

Other Technology Transfer Grants have supported further development of: antiviral drugs, a geriatric bed, an electronic calliper for researchers, an environmental chamber for researchers, and a home monitoring device for heart attack patients.

Raylo Chemicals, an Edmonton manufacturer of chemicals for pharmaceutical products, is active in the race for an **AIDS DRUG.** A Technology Transfer Grant supported their work on a cheaper process to produce the main starting ingredient of the experimental AIDS drug, AZT. Though overproduction by many companies collapsed the market for AZT, the process has proved useful in synthesizing another experimental AIDS drug.

Dr. Andy Hoffer has patented a **RESEARCH TECHNIQUE** to record electrical activity from sensory nerves with the aim of restoring function in paralyzed patients.

Dr. Tom Clandinin has a Canadian and an American patent for improvements to **INFANT FORMULAS.** The formulas were based on his studies of dietary fatty acid balance, work which he's applied to several health problems including diabetes.

Bringing Home the Bacon (To Alberta)

Scientists compete fiercely for finite research funds. Most grants are awarded on a peer review system. This means whether or not researchers get grants, depends upon how established people in the field judge their track records.

Therefore one way of assessing the quality of AHFMR scientists' work is to ask: "Are they successful in national and international granting competitions? Are they bringing outside funds back to Alberta?"

Yes, indeed they are, at unprecedented levels.

MAGIC BULLETS may be a powerful new weapon in the fight against cancer. "Magic bullets" is the nickname for monoclonal antibodies or MAbs. These are engineered antibodies which head directly to specific antigens on the surface of cells. Because some cancer cells have antigens not found on healthy cells, MAbs can be attached to fluorescent material and used to detect malignant cells.

Dr. Grant MacLean has successfully used a MAb to detect pelvic cancer earlier than conventional methods. Developed by Dr. Michael Longenecker and Dr. Tony Noujaim, the MAb also indicates how aggressive the cancer is, a help to physicians when choosing the best treatment. Dr. Grant MacLean and colleagues at the Cross Cancer Institute have received a University-Industry grant for $1.3 million from the Medical Research Council of Canada and Biomira, an Edmonton biotechnology company. The grant supports further clinical testing which will eventually be expanded to other centres across the country.

The brighter areas show the spread of lung cancer detected by a MAb.

The **NATIONAL INSTITUTES OF HEALTH (NIH)** in the U.S. is arguably the world's largest and most prestigious medical research organization. NIH has given Dr. Rufus Day III a three-year grant of $81,000 to study DNA repair in normal human cells and in tumor cells with a particular altered base.

Chemical masters of the brain called neurotransmitters play key roles in controlling many functions. Dr. Quentin Pittman has shown that one neurotransmitter helps regulate blood pressure and two others stop brain cell excitability in the hippocampus, an event which occurs with epilepsy. Dr. Pittman is one of several AHFMR researchers who have been awarded the prestigious position of **MEDICAL RESEARCH COUNCIL OF CANADA** Scientist.

Dr. Chris Bleackley

Dr. Chris Bleackley can show a video that looks exactly like an outer space arcade game. It's actually a video tape of killer cells in the immune system destroying target cells such as tumor cells or foreign cells from an organ transplant. Dr. Bleackley has discovered that two proteins are "shot out" into the target cells when the killer cell fuses to it. He has also isolated the genes which encode the proteins, important information for developing cancer immunotherapies and preventing rejection.

Dr. Bleackley received one of the largest 1988 operating grants from the **NATIONAL CANCER INSTITUTE** in Canada.

Dr. Tessa Gordon is finding out how some damaged nerves regrow back to muscle cells—sometimes the right ones and sometimes the wrong ones. Her innovative work on **NERVE REGENERATION** may lead to new drug therapy or physiotherapy to improve recovery after injury. In 1988 Dr. Gordon received over $250,000 in operating grants from four national agencies.

> *"In MRC's award competition this year (1989), candidates from Calgary came first and second and took four out of ten total awards in the scholarship competition for health professionals (which attracted 43 candidates and in which competition was particularly fierce)."*
>
> Dr. Pierre Bois
> President, Medical Research
> Council of Canada

Achievements:

- In 1988 AHFMR researchers attracted over $6 million in funding from outside sources
- Largely because of AHFMR funding, the University of Alberta moved from 11th position in 1987 to 4th in the ranking of Canadian medical colleges according to highest research expenditures. The University of Calgary moved from 15th position to 7th
- In 1988 the percentage increase of funding from the Medical Research Council of Canada was 15.4%, well ahead of any other universities in the country

Challenges:

- To use acquired funding wisely
- To continue supporting and training quality scientists who can attract a high level of operating grants

The Young and the Bright

ANTIDEPRESSANT DRUGS work for some patients, but nobody knows why. Dr. Andrew Greenshaw is finding out. His studies earned him the first Young Investigator Award given by the Canadian College of Neuropsychopharmacology. Dr. Greenshaw has developed an ingenious rat model of "depression" to study the effects of antidepressants on natural brain chemicals called neurotransmitters. He has discovered that a widely used class of drugs creates changes in these brain chemicals by an unexpected mechanism. This information can be exploited to design improved antidepressants.

In 1987 Dr. Thomas Reh was one of two Canadians awarded a prestigious Alfred P. Sloan Fellowship given to young scientists of extraordinary promise by the Sloan Foundation in New York. He uses the optic nerve of the frog to study **NERVE REGENERATION.** Epilepsy researcher, Dr. Brian MacVicar was the only Canadian to win a Sloan Fellowship in 1986.

Dr. John Bell and colleagues at Stanford made a significant discovery about the **RISK FOR DIABETES.** Replacement of a single amino acid in certain proteins which are important in the immune response greatly increases the risk. Dr. Bell is an AHFMR Fellow whose achievements have led to a prestigious position at Oxford University. Another young Alberta Fellow funded at Stanford, Dr. Brett Finlay has discovered how *Salmonella* bacteria become established in the body.

Two Clinical Fellows were honoured for their **STROKE RESEARCH.** Dr. Lew Disney received the 1987 Congress of Neurological Surgeons' resident award for showing a drug reduced brain damage after a ruptured aneurysm. Dr. Michael Nosko won the American Academy Neurology Award for showing early surgery to remove clots also helped. Dr. Mark Cattral earned the 1988 National Research Prize from the Canadian Association of General Surgeons for transplant studies.

Dr. Edward Tredget is studying the wound-healing process at the molecular level in **BURN VICTIMS.** He helped devise a new stable isotope technique to assess factors such as collagen metabolism so that physicians can assess which treatments are effective and devise new ones. A plastic surgeon from the U of A, Dr. Tredget received specialized research training at Harvard and has returned to establish a research program in the Fire Fighter's Burn Unit in Edmonton.

Fellows are young PhDs or MDs who receive further research training under the supervision of established scientists. Dr. Tredget is one of the Fellows who were sent abroad to gain expertise not available in Alberta and who then returned to establish new research programs as Heritage Medical Scholars in their own labs. Other examples are discussed elsewhere in this publication: Drs. Warnock and Kneteman (p. 5), Dr. Robert Berdan (p. 16), Dr. Cy Frank (p. 19).

Some **BRIGHT STUDENTS FUNDED BY AHFMR** make their mark early as well. While a PhD student, Les Nagata won an award from the American Society for Microbiology for work on the reovirus S1 gene. Catherine Field won the 1987 American Nutrition Graduate Study Research Prize for animal studies on the effects of fats on fat cells of diabetics.

Dr. Andy Greenshaw

Achievements:

- The young Scholars funded are beginning to earn honors for their work
- Since 1980, 860 Fellows and 2,100 Students have been supported in a training program which keeps the scientific community vigorous, keeps promising young people in Alberta, and which is critical to the productivity of established scientists
- The growing international reputation of Alberta's scientists attracts bright, young scientists to study with them
- Many AHFMR Fellows have moved on to prestigious positions in Alberta, the rest of Canada, and abroad
- Clinical Fellows are significantly bridging the gap between new knowledge in basic research and its application to patient care in clinical research

Challenges:

- To maintain the highest standards for recruiting young scientists
- To adequately fund a broad-based training program
- To provide the funding and the positions to keep outstanding young scientists in Alberta

Caring for Patients

> *"Let us at least help where we can, treat the symptoms, and help the family manage the patient."*
> Dr. Irma Parhad

THE DREADED ALZHEIMER'S DISEASE will strike at least seven percent of us after 65. The causes are unknown and there is no cure. Dr. Irma Parhad is one of the few North American physicians tackling the disease on all fronts: public education, patient and family care, and molecular research to understand the disease.

In 1985 she founded The University of Calgary Dementia Clinic. Because Alzheimer's is very difficult to diagnose (and in clinical practise is both under and over diagnosed) the first task is identifying the disease as distinct from other causes of dementia such as stroke or psychiatric problems. Dr. Parhad explains, "First, we have to be very strict with our criteria in diagnosing Alzheimer's disease. Second, we have to be understanding and give hope and encouragement to the patients and their families. Let us at least help where we can, treat the symptoms, and help the family manage the patient."

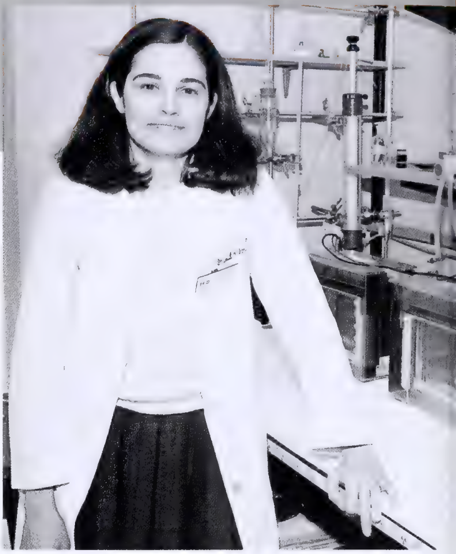
Patient data from the clinic is valuable to researchers everywhere. It is one of five Canadian centres studying familial Alzheimer's and will participate in large North American population studies of disease patterns.

In the lab Dr. Parhad studies how gene expression is controlled for proteins involved in the development of the neurofibrillary brain lesions which are characteristic of Alzheimer's disease. Some of her findings have relevance to ALS, another severe neurological disease.

Dr. Parhad emphasizes that emotional involvement with patients helps to give her research direction. "It's the patients and their families who give me the energy to remain positive," says Dr. Parhad. "You get to know these people: you are working with them and for them."

Dr. Derek Griffiths' new incontinence clinic at the Edmonton General Hospital focuses on one of the most distressing problems in **GERIATRIC ILLNESS.** He has developed new diagnostic techniques with innovative equipment he has designed. His studies suggest there are multiple causes of incontinence with various treatment options.

Dr. John Gill has established a multidisciplinary **AIDS CLINIC** in Calgary where patients are given the latest available therapies, mainly multi-centre trials for drugs such as AZT. Heterosexual transmission and the effects of other antiviral drugs are also studied. A new HIV culture facility allows Dr. Gill and others to conduct basic research on the virus. As an infectious disease specialist, Dr. Gill advises Southern Alberta physicians on how to care for difficult cases of various diseases.



Achievements:

- AHFMR researchers make the latest advances available to Alberta patients
- Researchers contribute significantly to the education of medical students and the continuing education of physicians
- 11 new specialty clinics have been established since 1980
- The AHFMR clinical research program with 23 clinical fellows and 20 clinical investigators (in 1989) and the multidisciplinary group structure ensure new knowledge is translated into patient care

Challenges:

- To maintain sufficient funding to continue attracting physicians to research
- To provide a protected environment while they acquire research skills
- To provide funding (or coordinate other sources of funding) and recruit trained personnel for: expensive and complex clinical trials, epidemiological studies, evaluation research and dissemination programs to health care professionals

Dr. Johny Van Aerde with a tiny newborn

Dr. Johny Van Aerde cares for the tiniest patients—premature babies, sometimes as small as 800 grams. He has created a **DESIGNER FORMULA** which increases infants' survival and apparently helps them grow and develop neurologically at a more normal rate. Based on information from basic studies of fatty acid metabolism, the formula may also be important as a supplement for breast fed babies.

MELANOMA PATIENTS at the Cross Cancer Institute are benefiting from Dr. Kowichi Jimbow's advanced diagnostic techniques. Commonly known as mole cancer, melanoma is deadly if not detected, but treatable in the early stages. Dr. Jimbow is finding a way to identify premalignant moles and he is also devising a new treatment for advanced melanoma.

KIDNEY TRANSPLANTS give patients with end stage renal disease new life and freedom from dialysis. Surgeon, Dr. Leendert Paul is Director of the Transplantation Clinic at the Foothills Hospital. In his basic immunology studies he is developing new ways to prevent rejection.

(For a more complete picture of patient care see Index to Patient Care p. 42)

Index to Patient Care

ALZHEIMER'S DISEASE: Dr. Irma Parhad— clinic for diagnosis & treatment (see p. 40).

ATHEROSCLEROSIS: Dr. Shinji Yokoyama—pioneer therapy (p. 10).

AUTISM: Dr. Cathy Lord, autism clinic & therapy groups (see p. 24).

ARTHRITIS: Dr. Cy Frank, patient clinic, joint surgery & pioneer therapy (see p. 19); Dr. Thomas Martin—assists surgeons; Others—drug studies.

BURN INJURIES: Dr. Edward Tredget—therapy.

CANCER: Dr. Peter Allen—MR studies (p. 27); Dr. Grant MacLean—MAb studies (p. 37); Dr. Kowichi Jimbow—melanoma; Dr. Malcolm Paterson—breast cancer prognosis (p. 30); Dr. Rene Lafreniere—pioneer immunotherapy & surgery.

CARDIAC DISEASE: Drs. George Wyse, Brent Mitchell, Anne Gillis—arrhythmia clinic (see p. 6); Dr. Henry Duff—drug development (p. 29); Drs. Bodh Jugdutt & David McPherson—echocardiography; Dr. Yashu Coe—infant cardiology; Dr. Frank Witkowski—cardiac clinic (see p. 26).

DIABETES: Drs. Norman Kneteman & Garth Warnock— transplant & other surgery (see p. 5); Dr. Edmond Ryan— pregnancy clinic; Dr. Leigh Field—risk assessment.

EPILEPSY: Dr. Neil Finer—neonatal seizures (p. 33); Dr. Penny Codding-drug development (p. 28).

GASTROINTESTINAL DISEASES: Dr. Brent Scott— pediatric clinic (p. 25); Dr. Richard Fedorak— diarrhea clinic and Crohn's disease trials; Dr. Joe Davison— collaborative trials; Dr. Diane Taylor—diagnostics for food poisoning.

GERIATRIC PROBLEMS: Dr. Derek Griffiths—incontinence clinic.

HEARING PROBLEMS: Dr. Jos Eggermont—diagnosis (see p. 27).

INFECTIOUS DISEASES: Drs. Dean Befus & Timothy Lee-collaborative parasitology studies; Dr. John Gill—AIDS clinic (p. 40); Dr. Jutta Preiksaitis—CMV patients.

KIDNEY TRANSPLANTS: Drs. Leendert Paul & Philip Halloran—surgeons.

LIVER DISEASE: Dr. Sam Lee—diagnosis.

LUNG DISEASES: Dr. Dale Lien—inflammatory lung disease; Drs. Malcolm King & Donald Woods—CF lung infections (p. 32); Dr. Francis Green—diagnosis of occupational lung disease.

LUPUS: Dr. Marvin Fritzler—diagnosis & care (p. 9).

METABOLISM & NUTRITION: Dr. Johny Van Aerde—neonatal care (p. 41); Dr. David Lau—obesity clinic; Dr. Floyd Snyder— inherited metabolic diseases.

SLEEP DISTURBANCES: Dr. John Remmers—sleep apnea (p. 34); Dr. James Fewell—crib death (p. 25).

STROKE THERAPY: Dr. Arthur Prochazka—therapy (p. 12); Dr. William Fletcher—diagnosis; Dr. Bruce Tranmer—therapy.

SPINAL-CORD INJURED PATIENTS: Drs. Arthur Prochazka, Richard Stein & Dejan Popovic—electrical therapy (p. 13).

THYROID DISORDERS: Dr. Norman Wong—endocrinology care.

Programs of the Foundation

Heritage Medical Scientist Awards

This award encourages the recruitment and establishment of senior medical scientists to Alberta. Heritage Medical Scientists are leaders in their fields and are internationally recognized for their scientific contributions. The award is for five years and renewable.

Scholarships

Heritage Medical Scholars are investigators recently trained in medical research who have demonstrated promise and ability to initiate and conduct independent research. A five-year, renewable Scholarship allows scientists to develop medical research unhampered by heavy teaching and service duties.

Clinical Investigatorships

Clinical Investigatorships give clinically qualified medical scientists holding full-time academic appointments further research training and experience assisted by competitively-funded basic or clinical researchers. Clinical investigators must have an M.D. or D.D.S., have completed clinical specialty training and two or three years of supervised medical research. The three-year award may be extended for three years but is not renewable.

Independent Establishment Grants for New Investigators

Independent Establishment Grants are given to new investigators who are not funded by the Foundation. The grant helps them quickly achieve maximum research productivity by providing equipment, technical assistance, and materials.

Fellowships

Heritage Medical Research Fellowships provide qualified candidates with full-time postdoctoral training in research in an area of medical science relevant to the aims of the Foundation. Fellows must have an M.D., D.D.S., D.V.M., Ph.D., or Pharm.D., and must demonstrate high academic standing and evidence of research ability.

Clinical Fellowships

Clinical Fellowships give individuals who have completed clinical training an opportunity to gain supervised medical research experience. Applicants must have a medical or dental degree and have completed subspecialty clinical training. This one-year award may be renewed four times.

Studentships

There are a limited number of full-time Studentships for students registered in full-time M.Sc. or Ph.D. programs, and who plan careers in medical research. A limited number of part-time Studentships are available to students working towards professional health-related degrees. Summer Studentship awards support promising Alberta university students from May to August.

Technology Transfer Grants

The Technology Transfer Program provides an opportunity for Alberta medical researchers or engineers to promote university-industrial collaboration in Alberta, stimulate technological innovation in Alberta, and advance medical research to the stage where private investors may provide seed capital.

Phase I grants enable applicants to strengthen the technical merit and explore the feasibility of a scientifically sound project. Phase II grants apply when a product or technique has been identified and laboratory tested but requires further investigation and refinement to attract seed/venture capital.

Visiting Scientists

Awards for Visiting Scientists to Alberta enable a limited number of highly innovative and productive medical scientists to engage in medical research in an Alberta university for the purpose of bringing special knowledge and expertise to the host department, group, or institution.

Awards for Visiting Scientists from Alberta enable Alberta medical scientists to undertake collaborative research which they are unable to undertake locally due to inadequate technology or collegial expertise.

Conference Grants

The Foundation supports a limited number of conferences and workshops clearly related to the enhancement of medical research in Alberta and the transmission of significant new knowledge to those who care for patients.

Visiting Lecturers

The Visiting Lecturer program helps Alberta universities attract outstanding medical scientists who can broaden and enrich the educational experience of graduate students and fellows. The program also gives Alberta investigators opportunities to discuss their research with others in their field.

Travel Grants

The Foundation annually gives Travel Grants to the U of A and the U of C to be administered by the Universities to faculty for: attending workshops, conferences, and annual meetings; recruiting researchers; briefly visiting other laboratories to study new techniques or discuss collaborations.

Visiting Professors

Heritage Medical Research Visiting Professorships are available to attract truly outstanding medical scientists to visit Alberta to enrich and enhance the climate of medical research.

Grants for Major Equipment

Major Equipment grants and equipment maintenance funds permit the university on behalf of investigators to purchase and maintain equipment essential to high-quality research. Applications usually relate directly to research projects supported by competitive granting agencies.

Preference is given to expensive facilities providing support to groups of researchers and multidisciplinary projects, especially those facilities offering services to researchers with partial or full recovery arrangement for operating costs.

Institutional Grants

Institutional Grants to the Universities cover some of the costs associated with an influx of AHFMR scientists and include items such as renovations, recruiting costs, support staff, library grants, and special initiative grants.

Personnel

HERITAGE MEDICAL SCIENTISTS

ALLEN, Peter, Ph.D., Department of Applied Sciences in Medicine, Faculty of Medicine, University of Alberta "Imaging and Biochemical Applications of NMR to Medicine"

BRINDLEY, David, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Control of Glycerolipid and Lipoprotein Metabolism"

DAVISON, Joseph, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Nervous Control of Gastrointestinal Secretions"

GILES, Wayne, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Electrophysiology-Pharmacology of Rabbit and Human Cardiac Cells"

GRIFFITHS, Derek, Ph.D., Department of Applied Sciences in Medicine, Faculty of Medicine, University of Alberta "Urodynamics"

HULLIGER, Manuel, Ph.D., Departments of Clinical Neurosciences and Medical Physiology, Faculty of Medicine, University of Calgary "Peripheral Control of Voluntary Movement in Man and Cat"

JIMBOW, Kowichi, M.D., Ph.D., Department of Medicine, Faculty of Medicine, University of Alberta "Melanogenesis and Laboratory Diagnosis and Rational Therapy of Malignant Melanoma"

*__MALONEY__, John, Ph.D., Department of Obstetrics and Gynecology, Faculty of Medicine, University of Calgary "The Physiology and Development of the Fetus and Neonate"

McGHEE, James, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Gene Expression During Animal Development"

PATERSON, Malcolm, Ph.D., Department of Medicine, Cross Cancer Institute "Clinical Genetics and Molecular Carcinogenesis"

PAUL, Leendert, M.D., Ph.D., Department of Medicine, Faculty of Medicine, University of Calgary "Organ Transplant: Program of Clinical and Experimental Research"

RABINOVITCH, Alexander, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Immunobiology of Diabetes Mellitus"

REMMERS, John, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Control of Breathing by the Nervous System"

SALMI, Aimo, M.D., Ph.D., Department of Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "Immunopathogenesis of Neurovirological Diseases"

TER KEURS, Henk, M.D., Ph.D., Departments of Medicine and Medical Physiology, Faculty of Medicine, University of Calgary "Activation and Contraction of the Heart"

TYBERG, John, M.D., Ph.D., Departments of Medicine and Medical Physiology, Faculty of Medicine, University of Calgary "Cardiac Mechanics: Factors Affecting the Heart's Pumping Action"

VANCE, Dennis, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Phospholipid and Lipoprotein Metabolism"

WANG, Jerry, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Studies in Cell Regulation"

YOON, Ji-Won, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Two Possible Mechanisms for the Pathogenesis of Virus-Induced Diabetes Mellitus"

HERITAGE MEDICAL SCHOLARS

ACHESON, Ann, Ph.D., Department of Anatomy and Cell Biology, Faculty of Medicine, University of Alberta "Role of Cell Adhesion in Neurotransmitter Phenotypic Expression"

ANDERSON, M. John, Ph.D., Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary "Development of the Neuromuscular Junction"

ANDERSON, Robert, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Control of Virus Synthesis and Assembly"

AUER, Roland, Ph.D., M.D., Department of Pathology, Faculty of Medicine, University of Calgary "Neuronal Death in Ischemia, Hypoglycemia, and Epilepsy"

BAZETT-JONES, David, Ph.D., Departments of Anatomy and Medical Biochemistry, Faculty of Medicine, University of Calgary "Ultrastructure of Transcription Complexes"

BEFUS, Dean, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Studies of Intestinal Immunity and Mast Cells"

BENISHIN, Christina, Ph.D., Department of Physiology, Faculty of Medicine, University of Alberta "Presynaptic Modulation of Potassium Channels"

BERDAN, Robert, Ph.D., Department of Physiology, Faculty of Medicine, University of Alberta "Formation and Function of Electrical Synapses"

*__BIDDLE__, Fred, Ph.D., Departments of Pediatrics and Medical Biochemistry, Faculty of Medicine, University of Calgary "Genetic Studies of Threshold Traits of Mammalian Development"

*__BLASDEL__, Gary, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Development of Thalamocortical Afferents"

BLEACKLEY, Robert, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Molecular Genetics of T-Cell Differentiation"

BOISVERT, Donald, Ph.D., M.D., Department of Surgery, Faculty of Medicine, University of Alberta "Pathophysiology and Therapy of Cerebrovascular Occlusion"

*__BOURNE__, Gregory, Ph.D., Department of Physiology, Faculty of Medicine, University of Alberta "The Regulation of Testicular GnRH Receptors and GnRH-like Peptides and Their Roles in Steroidogenesis"

BOWLING, Douglas, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Projections of Single Identified Retinal Axons"

BULLOCH, Andrew, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Cellular Basis of Adult Neuronal Plasticity"

CAMPENOT, Robert, Ph.D., Department of Anatomy and Cell Biology, Faculty of Medicine, University of Alberta "Control of Nerve Fiber Growth and Survival by Ions, Pharmacological Agents and Electrical Activity"

*__CARNE__, Thomas, Ph.D., Department of Chemistry, Faculty of Science, University of Calgary "Biosynthesis of Pituitary Hormones"

CLANDININ, Michael, Ph.D., Departments of Foods and Nutrition and Medicine, Faculties of Home Economics and Medicine, University of Alberta "Nutrition and Metabolism of Dietary Fat"

CODDING, Penelope, Ph.D., Departments of Chemistry and Pharmacology and Therapeutics, Faculties of Science and Medicine, University of Calgary "Molecular Structure and Function Studies of CNS Active Drugs and Toxins"

COLMERS, William, Ph.D., Department of Pharmacology, Faculty of Medicine, University of Alberta "Neuromodulation in CNS"

** No longer funded by AHFMR under this award*

* **DANIELSON**, Terry, Ph.D., Department of Pharmacy and Pharmaceutical Sciences, Faculty of Pharmacy, University of Alberta "Metabolism and Plasma Levels of Clinical Monoamine Oxidase Inhibitors"

* **DASGUPTA**, Mrinal, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "MBP-Specific CIC in Multiple Sclerosis"

DAY III, Rufus, Ph.D., Department of Medicine, Cross Cancer Institute "DNA Repair and Gene Regulation in Human Tumor Systems"

DELAY, Michael, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Excitation-Contraction Coupling in Muscle"

DUFF, Henry, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Mechanistic Approach to Antiarrhythmic Therapy"

EASTON, Paul, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Hypoxia, Respiratory Muscles and Ventilatory Control"

EGGERMONT, Jos, Ph.D., Department of Psychology, Faculty of Social Sciences, University of Calgary "Functional Plasticity of the Auditory Nervous System"

FAMIGLIETTI, Edward, M.D., Ph.D., Department of Anatomy, Faculty of Medicine, University of Calgary "Functional Architecture of Vertebrate Retina"

FEWELL, James, Ph.D., Departments of Obstetrics and Gynecology and Medical Physiology, Faculty of Medicine, University of Calgary "Cardiorespiratory Control During Sleep"

FIELD, L. Leigh, Ph.D., Department of Pediatrics, Faculty of Medicine, University of Calgary "The Genetics of Susceptibility to Insulin-Dependent Diabetes"

FINEGOOD, Diane, Ph.D., Departments of Medicine and Physiology, Faculty of Medicine, University of Alberta "Hepatic Insulin Action and Insulin Resistance"

* **FORD**, Gordon, M.D., Department of Internal Medicine, Faculty of Medicine, University of Calgary "Interdependence of the Lung, Ribcage and Diaphragm During Atelectasis"

FOTEDAR, Arun, Ph.D., M.D., Department of Immunology, Faculty of Medicine, University of Alberta "T-Cell Recognition"

FRANK, Cyril, M.D., Ph.D., Department of Surgery, Faculty of Medicine, University of Calgary "Connective Tissue Structure and Function"

FRENCH, Robert, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Ionic Channels in Excitable Membranes"

FRITZLER, Marvin, Ph.D., M.D., Departments of Medicine and Medical Biochemistry, Faculty of Medicine, University of Calgary "Antinuclear Antibodies in Autoimmune Diseases"

FUJITA, Donald, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Control of Oncogene Activity"

GALLIN, Warren, Ph.D., Department of Zoology, Faculty of Science, University of Alberta "Cellular Mechanisms of Development"

GARBER, Anthony, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "The Molecular Biology of Psoriasis"

GELLMAN, Reuben, Ph.D., Departments of Clinical Neurosciences and Medical Physiology, Faculty of Medicine, University of Calgary "Processing of Oculomotor Signals in the Cerebellum"

GODBOUT, Roseline, Ph.D., Department of Anatomy & Cell Biology, Faculty of Medicine, University of Alberta "Molecular Genetics of Retinal Development"

GORDON, Tessa, Ph.D., Department of Pharmacology, Faculty of Medicine, University of Alberta "Neuromuscular Plasticity"

GREEN, Douglas, Ph.D., Department of Immunology, Faculty of Medicine, University of Alberta "Immunoregulatory T-Cells and Molecules"

GREEN, Francis, M.D., Ph.D., Department of Pathology, Faculty of Medicine, University of Calgary "Mechanisms of Lung Injury by Environmental Agents"

GREENSHAW, Andrew, Ph.D., Department of Psychiatry, Faculty of Medicine, University of Alberta "Beta Phenylethylamine, p-Tyramine and p-Octopamine and the Treatment of Affective Disorders"

* **HANGARTNER**, Thomas, Ph.D., Department of Applied Sciences in Medicine, Faculty of Medicine, University of Alberta "Development of Methods to Diagnose and Treat Bone Disorders"

* **HANLEY**, David, M.D., Department of Internal Medicine, Faculty of Medicine, University of Calgary "Studies of Parathyroid Hormone Physiology"

HART, David, Ph.D., Departments of Medicine and Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Immunochemical Characterization of Plasminogen Activators"

* **HICKS**, T. Philip, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Identification of Synaptic Transmitters in the Mammalian Visual and Somatosensory Systems"

* **HINDSGAUL**, Ole, Ph.D., Department of Chemistry, Faculty of Science, University of Alberta "Biological Recognition of Complex Carbohydrates"

* **HOAR**, David, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "DNA Sequence Diversity in Man"

HOFFER, J. Andy, Ph.D., Departments of Medical Physiology and Clinical Neurosciences, Faculty of Medicine, University of Calgary "Neural Control of Movements"

HULBERT, William, Ph.D., Department of Medicine, Faculty of Medicine, University of Alberta "The Effect of H_2S on Airway Structure and Function"

IATROU, Kostas, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "The Organization, Expression and Evolution of Eukaryotic Multigene Families in Chorion of *Bombyx Mori*"

JACOBS (KAUFMAN), Susan, Ph.D., Department of Medicine, Faculty of Medicine, University of Alberta "Control Mechanisms of Fluid and Electrolyte Balance"

* **JARVIS**, Simon, Ph.D., Department of Physiology, Faculty of Medicine, University of Alberta "Molecular Properties and Regulation of the Nucleoside Transport System"

* **JAWORSKI**, Maxine, M.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Pathogenesis of Insulin Dependent Diabetes Mellitus"

JENSEN, Susan, Ph.D., Department of Medical Microbiology and Infectious Diseases, Faculty of Science, University of Alberta "Biosynthesis of Novel Penicillin and Cephalosporin Antibiotics"

JUGDUTT, Bodh, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Modification of Ventricular Shape and Function During Healing After Myocardial Infarction"

KING, Malcolm, Ph.D., Department of Medicine, Faculty of Medicine, University of Alberta "Studies on Mucus Clearance"

KOOPMANS, Henry, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "The Internal Control of Food Intake"

LAFRENIERE, Rene, M.D., Department of Surgery, Faculty of Medicine, University of Calgary "Adoptive Immunotherapy of Tumors with Activated Lymphocytes and Biological Response Modifiers"

LAU, David, M.D., Ph.D., Department of Medicine, Faculty of Medicine, University of Calgary "Regulation of Adipose Tissue Development and Growth"

LEE, Patrick, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "The Mechanism of Virus Attachment of Host Cells"

* **LEE**, Timothy, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Protective Immunity to Nematode Infection"

* **LEFEBVRE**, Yvonne, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Passage of Steroid and Thyroid Hormones Across the Nuclear Envelope of Mammalian Cells"

* **LEUNG**, Wai-Choi, Ph.D., Departments of Medicine and Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "Molecular Cloning of Viral Neutralization Antigen and Human Tumor Antigen"

LOPASCHUK, Gary, Ph.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Fatty Acid Metabolism in the Heart"

LORD, Catherine, Ph.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Sex Differences in Autism"

MacVICAR, Brian, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Neuronal Basis for Synchrony During Seizure"

* **MANNONI**, Patrice, M.D., Department of Pathology, Faculty of Medicine, University of Alberta "Antigen Characteristics of Hematopoietic Stem Cells"

MANTLE, Michele, Ph.D., Departments of Medical Biochemistry and Pediatrics, Faculty of Medicine, University of Calgary "Structure, Synthesis and Secretion of Intestinal Mucus"

MIRANDA, Bruno, Ph.D., Department of Surgery, Faculty of Medicine, University of Alberta "Immuno-Cytochemical Investigation of Axonal Transport"

MARTIN, Renée, Ph.D., Department of Pediatrics, Faculty of Medicine, University of Calgary "Cytogenetic Analysis of Human Sperm"

MARTIN-IVERSON, Mathew, Ph.D., Department of Psychiatry, Faculty of Medicine, University of Alberta "Behavioral Functions of Dopamine Receptor Subtypes: Animal Models of Schizophrenia, Parkinson's Disease and Stimulant Addiction"

* **MATHESON**, David, M.D., Departments of Pediatrics and Internal Medicine, Faculty of Medicine, University of Calgary "Cellular Regulation of Immune Responses"

McFADDEN, Grant, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Molecular Biology of Tumorogenic Shope Fibroma Poxviruses"

McGARRY, Ronald, Ph.D., Department of Pediatrics, Faculty of Medicine, University of Calgary "Functional Role of MAG"

* **McPHERSON**, David, M.D., Department of Internal Medicine, Faculty of Medicine, University of Calgary "Cardiac Evaluation with Ultrasound"

MICHALAK, Marek, Ph.D., Departments of Pediatrics and Biochemistry, Faculty of Medicine, University of Alberta "Ca Transport Systems in Mature and Developing Heart"

MILLER, Freda, Ph.D., Department of Anatomy and Cell Biology, Faculty of Medicine, University of Alberta "Molecular Analysis of Neuronal Development"

* **MILLER**, Rodman, Ph.D., Department of Anatomy, Faculty of Medicine, University of Calgary "Freeze Fracture Localization of Antigens and of Cholesterol"

* **MILOS**, Nadine, Ph.D., Department of Anatomy and Cell Biology, Faculty of Medicine, University of Alberta "Factors Controlling Pattern Formation by Neural Crest Cells"

* **MINUK**, Gerald, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Role of GABA in Liver Disease"

MITCHELL, L. Brent, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Prophylactic Therapy for Ventricular Tachyarrhythmias"

MOORE, Graham, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "The Synthesis and Evaluation of Peptide Hormones and Analogues"

* **MORTIMER**, David, Ph.D., Departments of Obstetrics and Gynecology and Medical Physiology, Faculty of Medicine, University of Calgary "Human Sperm Physiology and Infertility"

NEWMAN, Stephen, M.D., Department of Psychiatry, Faculty of Medicine, University of Alberta "Mortality of Affective Disorder Patients in Alberta"

* **NORTHUP**, John, Ph.D., Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary "GTP Binding Proteins and Adenylate Cyclase"

PALCIC, Monica, Ph.D., Department of Food Science, Faculty of Agriculture/Forestry, University of Alberta "Enzyme Inhibitors as Therapeutic Agents"

PARHAD, Irma, M.D., Departments of Pathology and Clinical Neurosciences, Faculty of Medicine, University of Calgary "Neurofibrillary Degeneration: Pathogenic Mechanisms"

* **PARSONS**, Howard, M.D., Department of Pediatrics, Faculty of Medicine, University of Calgary "Energy Expenditure and Fatty Acid Metabolism"

PITTMAN, Quentin, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Peptide Neurotransmission in Brain"

PREIKSAITIS, Jutta, M.D., Departments of Medicine and Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "Transfusion Acquired Cytomegalovirus Infection: Epidemiology and Immune Response in Man"

PROCHAZKA, Arthur, Ph.D., Department of Physiology, Faculty of Medicine, University of Alberta "Neural Control of Mammalian Movement"

* **QUANDT**, Fred, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Electrical Properties of Isolated Retinal Neurons"

RAMCHARAN, Savitri, M.D., Ph.D., Department of Community Health Sciences, Faculty of Medicine, University of Calgary "Epidemiologic Studies of the Menstrual Cycle and PMS"

RATTNER, Jerome, Ph.D., Departments of Medical Biochemistry and Anatomy, Faculty of Medicine, University of Calgary "High Order Structure of Chromosomes"

READ, Randy, Ph.D., Department of Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "Protein Crystallography and Rational Design of Trypanocidal Drugs"

REH, Thomas, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Regeneration of Optic Nerve"

REHA-KRANTZ, Linda, Ph.D., Department of Genetics, Faculty of Science, University of Alberta "The Biochemical Basis of Mutation"

* **REITHMEIER**, Reinhart, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Structure and Function of Membrane Proteins"

REYNOLDS, John, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Studies of the Intestinal Immune System"

RORSTAD, Otto, M.D., Ph.D., Department of Medicine, Faculty of Medicine, University of Calgary "Mechanisms of Action of Brain Peptides"

RYAN, Robert, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Hormone-Induced Diacylglycerol Transport and Metabolism"

SCHNEIDER, Wolfgang, Ph.D., Department of Biochemistry, Faculty of Medicine, University of Alberta "Receptor-Mediated Endocytosis in Oocytes"

SCHNETKAMP, Paul, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Visual Transduction in Rod Photoreceptors"

SCHÜRCH, Samuel, Ph.D., Departments of Medicine and Medical Physiology, Faculty of Medicine, University of Calgary "Lung Stability and Cell Adhesion"

SEVERSON, David, Ph.D., Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary "Lipid Metabolism in Heart and Blood Vessels"

SINGH, Bhagirath, Ph.D., Department of Immunology, Faculty of Medicine, University of Alberta "Mechanism and Regulation of Antigen Recognition by T-Lymphocytes"

SMITH, Peter, Ph.D., Department of Pharmacology, Faculty of Medicine, University of Alberta "Electrophysiological Studies of the Electrogenic Sodium Pump in Sympathetic Ganglia and Spinal Cord"

SNYDER, Floyd, Ph.D., Departments of Medical Biochemistry and Pediatrics, Faculty of Medicine, University of Calgary "Studies of Inherited Disorders of Nucleotide Metabolism"

SOKOL, Pamela, Ph.D., Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary "Role of Iron in the Pathology of *Pseudomonas* Infection"

STOCKBRIDGE, Norman, M.D., Ph.D., Department of Surgery, Faculty of Medicine, University of Alberta "Signal Processing by Neurons"

TAYLOR, Diane, Ph.D., Department of Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "Characterization of Bacterial Plasmids"

* **TRAYHURN**, Paul, Ph.D., Departments of Medicine and Foods and Nutrition, Faculty of Medicine, University of Alberta "Regulation of Energy Balance"

* **TYLER**, Jonathan, Ph.D., Department of Genetics, Faculty of Science, University of Alberta "Structure and Function of Biological Membranes"

VOGEL, Hans, Ph.D., Department of Biochemistry and Biological Sciences, Faculty of Science, University of Calgary "NMR Studies of Mechanistic and Regulatory Aspects of Metabolism"

WAISMAN, David, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Studies of Calcium Binding Proteins"

WALLACE, John, Ph.D., Department of Medical Physiology, Faculty of Medicine, University of Calgary "Endogenous Mediators of Gastrointestinal Pathophysiology"

WALSH, Michael, Ph.D., Department of Medical Biochemistry, Faculty of Medicine, University of Calgary "Enzyme Regulation by Calcium"

WENMAN, Wanda, M.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Human Infections with *Chlamydia Trachomatis*"

WITKOWSKI, Francis, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Autonomic Neural Influences in Arrhythmogenesis"

WONG, Norman, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Mechanism of Thyroid Hormone Action"

WONG, Sui-Lam, Ph.D., Department of Biological Sciences, Faculty of Science, University of Calgary "Gene Regulation and Secretion in *Bacillus Subtilis*"

WOODS, Donald, Ph.D., Department of Microbiology & Infectious Diseases, Faculty of Medicine, University of Calgary "Pathogenesis of *Pseudomonas Aeruginosa* Disease"

WYSE, George, Ph.D., M.D., Departments of Medicine and Pharmacology and Therapeutics, Faculty of Medicine, University of Calgary "Investigations in Hypertension and Electrophysiology"

YOKOYAMA, Shinji, M.D., Ph.D., Department of Medicine, Faculty of Medicine, University of Alberta "Mechanism of Reverse Cholesterol Transport"

ZWIERS, Hindrik, Ph.D., Departments of Medical Physiology and Medical Biochemistry, Faculty of Medicine, University of Calgary "Neuropeptides, Phosphoproteins, and Neural Plasticity"

■ HERITAGE CLINICAL INVESTIGATORS

* **BEAUCHENE**, James, M.D., Department of Surgery, Faculty of Medicine, University of Alberta "Biological Basis of Therapeutic Tissue Expansion"

BERTHIAUME, Yves, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Mechanisms of Alveolar Liquid Clearance"

COE, James, M.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Pharmacological Manipulation of the Neonatal Circulation"

FEDORAK, Richard, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Adaptation and Regulation of Intestinal Glucose Transport"

FLETCHER, William, M.D., Department of Clinical Neurosciences, Faculty of Medicine, University of Calgary "Visual Motor Dysfunction with Frontal Lobe Lesions"

GILL, M. John, M.D., Departments of Microbiology and Infectious Diseases and Medicine, Faculty of Medicine, University of Calgary "Investigations of Viral Pathogenesis"

GILLIS, Anne, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Myocardial Kinetics and Pharmacodynamics"

HO, May, M.D., Department of Microbiology and Infectious Diseases Faculty of Medicine, University of Calgary "Immunoregulation in *P. Falciparum* Malaria"

KNETEMAN, Norman, M.D., Department of Surgery, Faculty of Medicine, University of Alberta "Islet Isolation, Immunodulation and Immunosuppression"

KUNIMOTO, Dennis, M.D., Department of Medical Microbiology and Infectious Diseases, Faculty of Medicine, University of Alberta "IgA Regulation"

LEE, Samuel, M.D., Department of Internal Medicine, Faculty of Medicine, University of Calgary "Pathophysiology of Portal Hypertension"

LIEN, Dale, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Neutrophils in Airway Inflammation"

MACLEAN, Grant, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Monoclonal Antibodies in Small Cell Lung Cancer"

MEDDINGS, Jonathan, M.D., Department of Medicine, Faculty of Medicine, University of Calgary "Physiology of Intestinal Permeability"

PARFREY, Nollaig, M.D., Department of Pathology, Faculty of Medicine, University of Alberta "Immune Mechanisms in Self Tolerance and Autoimmunity"

RYAN, Edmond, M.D., Department of Medicine, Faculty of Medicine, University of Alberta "Insulin Resistance in Pregnancy"

SCOTT, R. Brent, M.D., Department of Pediatrics, Faculty of Medicine, University of Calgary "Gastrointestinal Motor Function"

TRANMER, Bruce, M.D., Department of Clinical Neurosciences, Faculty of Medicine, University of Calgary "The Role of Hypervolemic Hemodilution During Cerebral Ischemia"

TREDGET, Edward, M.D., Department of Surgery, Faculty of Medicine, University of Alberta "Collagen Metabolism *In Vivo*"

VAN AERDE, Johny, M.D., Department of Pediatrics, Faculty of Medicine, University of Alberta "Fat Utilization in Parenterally Fed Newborn Infants"

WARNOCK, Garth, M.D., Department of Surgery, Faculty of Medicine, University of Alberta "Transplantation of Human Islets of Langerhans"

■ OTHERS:

BELL, John, Department of Medicine, Oxford, England (Fellowship 83-85)

DAVIS, Lyle, M.D., Professor of Surgery, University of Alberta

DISNEY, Lew, M.D., Division of Neurosurgery, Faculty of Medicine, University of Alberta (Fellowship 83-87)

FIELD, Catherine, Department of Medicine, Faculty of Medicine, University of Alberta (Studentship 84-87)

FINER, Neil, M.D., Professor, Department of Pediatrics, Royal Alexandra Hospital (Special Initiative Grant)

HALLORAN, Philip, M.D., Ph.D., Professor of Nephrology, Head of the Kidney Transplant Program, University of Alberta (Establishment Grant)

HODGES, Robert S., Ph.D., President, Synthetic Peptides Incorporated and Professor, Department of Biochemistry, University of Alberta (Technology Transfer and Major Equipment Grants)

MARTIN, Thomas, Ph.D., Assistant Professor, Faculty of Rehabilitation Medicine (Establishment Grant)

NAGATA, Les, Ph.D., Department of Microbiology, University of Southern California (Studentship 82-87 and Fellowship 87-89)

NOSKO, Michael, Ph.D., Division of Neurosurgery, Faculty of Medicine, University of Alberta (Fellowship 83-86)

PANG, Peter, Ph.D., Director, The Traditional Chinese Medicine Program and Professor and Chairman, Department of Physiology, University of Alberta (Establishment Grant)

PARKER, J.M. Robert, Ph.D., Research Associate, Department of Biochemistry and Vice President of Research, Synthetic Peptides Incorporated, University of Alberta (Technology Transfer Grant)

PEPPLER, Mark, Ph.D., Assistant Professor, Department of Medical Microbiology and Infectious Diseases, University of Alberta (Establishment Grant)

POPOVIC, Dejan, Ph.D., Professor, Division of Neurosciences and AHFMR Visiting Scientist to Alberta & Professor, Department of Electrical Engineering, University of Alberta, Belgrade, Yugoslavia (Visiting Scientist to Alberta)

RAJOTTE, Ray, Ph.D., Associate Professor, Department of Endocrinology, University of Alberta (Establishment & Technology Transfer Grants)

SCHRYVERS, Anthony, M.D., Ph.D., Assistant Professor, Department of Microbiology and Infectious Diseases, University of Calgary (Fellowship 82-85, and Establishment Grant)

SHRIVE, Nigel, Ph.D., Adjunct Associate Professor, Departments of Surgery and Civil Engineering, University of Calgary

STEIN, Richard, Ph.D., Director of AHFMR Neurosciences group, and Professor, Department of Physiology, University of Alberta (Technology Transfer and Major Equipment Grants)

TULIP, John, Ph.D., Professor, Department of Electrical Engineering, University of Alberta (Technology Transfer Grant)

WANG, Lawrence, Ph.D., Co-Director, The Traditional Chinese Medicine Program and Professor, Department of Zoology, University of Alberta (Establishment Grant)

The Revolution Continues

.....Uncovering secrets of gene, molecule, and cell remains our best hope for preventing disease.

The Vision has Materialized

.....Many Alberta scientists are internationally recognized for their leading research.

The Vehicle has Worked

.....AHFMR programs have attracted and supported a critical mass of excellent researchers.

The People are in Place

.....They've achieved many little breakthroughs and more researchers are waiting to join them for the big breakthroughs.

But the Funds are not sufficient

.....To keep up the momentum of activity and reap the benefits of the remarkable progress so far.

The Result:

.....Researchers work and wait on the edge of discovery, hoping to be adequately supported for the big breakthroughs which will lead to better health for all.

ON THE EDGE

The Story of The Alberta Heritage Foundation for Medical Research

3125 ManuLife Place, 10180 - 101 Street, Edmonton,
Alberta T5J 3S4 Telephone: (403) 423-5727

The Story of AHFMR

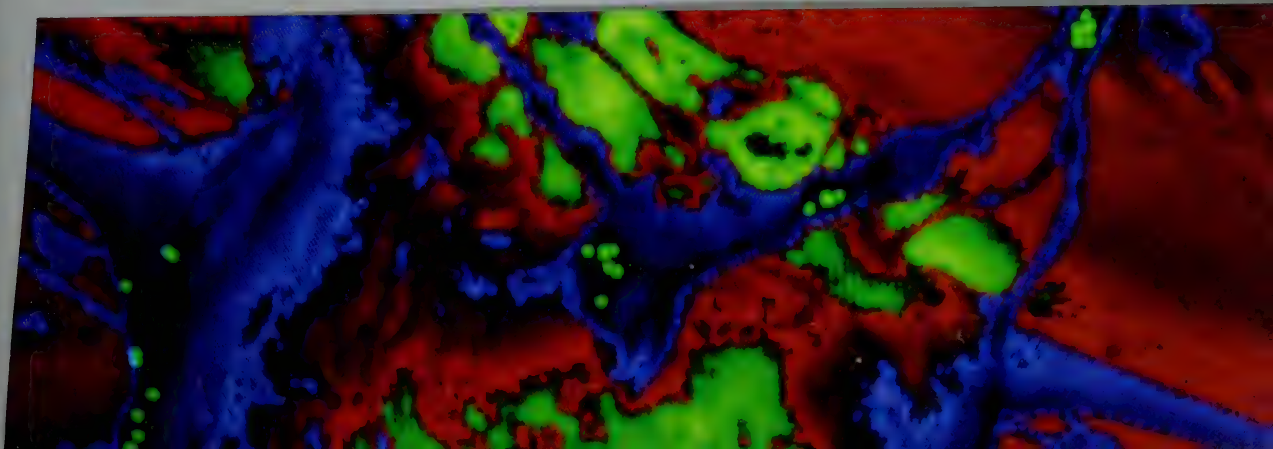
The Alberta Heritage Foundation for Medical Research is a bold experiment that worked. Whether Albertans and the rest of the world will receive the full benefits of the experiment is an open question.

■ **IN 1979 IT WAS A DREAM**—to make Alberta a world centre of medical research. The far-reaching vision was largely The Hon. Peter Lougheed's, who was Premier of Alberta at the time. Staff in medicine and science at the universities of Alberta and Calgary had come to him with a problem and plea for funds. There were islands of excellence among medical researchers in the province but activity was distressingly sparse and inadequately supported. The severe shortage of well-trained researchers weakened the quality of medical education and patient care. Hon. Lougheed and his government decided not only to solve these problems, but to go a step further and create a large base of superior medical researchers whose achievements could benefit the world.

■ **WHAT WAS NEEDED?** To find the answer, Hon. Lougheed consulted with people in the universities, health care institutions and business communities. Medical research activity was also surveyed in the rest of Canada and other countries with the help of Dr. Jack Bradley who later became Executive Director of AHFMR.

People in the scientific communities everywhere generally agreed upon what would make the ideal research environment:

Funding must be secure and long-term because research is a long-term investment and researchers need time to become established. Medical research is an expensive, competitive activity so funding must be more than adequate. It must be generous to attract the best researchers and give them the necessary technological support to do their work. Support must be based on the most promising basic sciences rather than targeted, disease-oriented research or politically motivated research which U.S. experience had shown does not work well. Decisions about what research is supported should be independent of the government and made by the scientists' peers. The research funded should meet the highest international standards of excellence. There must be a way to encourage and support clinical research. To maintain the vitality of a creative, productive research community, there must be sound training programs for bright, young people.



THE VEHICLE FOR THE DREAM WAS THE ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH established by an Act of Legislature in 1979. Its mandate was unequivocal: To establish and support a balanced, long-term program of medical research based in Alberta directed toward the discovery of new knowledge and the application of that new knowledge to improve the health of Albertans and all people.

AHFMR was given an initial endowment of $300 million, to be assessed for its adequacy after six years. Operations would be funded from the investment earnings of the endowment so that it remained intact.

The Foundation was carefully designed to be at arms-length from the government. It would be run by a board of trustees with representatives from the universities, the medical profession and the general community. An international scientific advisory committee would advise on policy and major funding thrusts to ensure activities supported are of the highest standards. In addition, every six years an International Board of Review must assess the productivity and effectiveness of AHFMR.

IT WAS A BOLD EXPERIMENT—an investment in knowledge and brain power. Alberta would keep its best scientific minds at home and attract more of the world's finest. Some people weren't sure it would work. Would people move to Alberta from London, Paris, Boston, Tokyo, Auckland, New York?

It worked and they came. Since 1980 the Foundation has recruited over 170 senior scientists from throughout North America, Europe, Asia, Australia and New Zealand. They've been attracted by generous funding, protected time for research, relative freedom to pursue their ideas, and the opportunity to work in a growing community of esteemed senior scientists and bright young people.

AHFMR IS AN ANOMALY. Over and over new scientists say, "There aren't opportunities like this elsewhere."

As the third Triennial Report shows, scientists have made the most of their opportunities. Many have been recognized internationally for their work in a wide variety of disciplines. Previous areas of strength such as biochemistry are even stronger. Other entirely new areas such as occupational lung disease, Alzheimer's disease, autism, and advanced immunology studies are new to Alberta.

Higher ratings of universities and new patient clinics are two kinds of concrete evidence which shows AHFMR scientists have significantly improved the quality of medical education and patient care.

Their innovations have also been catalysts for new research-related industry and begun to fulfill one of the original hopes in establishing the Foundation, the hope that Alberta's economic base would be broadened by spin-off activity.

FLEXIBILITY has been key. Until 1987 AHFMR was able to create and support programs needed to establish the research community and create the research environment envisioned in 1979. Support included the following:

Equipment grants given to almost every scientific department at the universities with a longstanding technological deficit. ■ AHFMR scientists and others were given establishment grants to build new research programs. ■ The universities were given institutional grants to help cover the associated costs of more personnel and new programs. ■ When an emerging group needed a prestigious scientist with a specific expertise, he or she was offered an agreement that competed with offers from long-established, leading research centres in the world. ■ An extensive educational and training program for Fellows and Students was established. ■ When existing facilities were inadequate for new personnel, two AHFMR research buildings were built, one at the U of C and one at the U of A. ■ To address the paucity of well-trained clinical researchers AHFMR created a clinical research program that was unique in Canada and the world. ■ AHFMR was one of the first Canadian funding agencies to establish a technology transfer program to assist people in universities and private industry to take innovations from the laboratory to the marketplace. ■ When other special needs or opportunities arose, AHFMR funded conferences, visiting scientists to and from Alberta, and special initiatives.

THIS FLEXIBILITY AND PROTECTION OF THE FULL RANGE OF FOUNDATION PROGRAMS ARE NOT GUARANTEED FOR THE FUTURE unless the original endowment is supplemented. Increased funds are also essential to maintain the momentum and take the next steps towards health care advances. These critical steps are: consolidating multidisciplinary groups; accelerating the development of patient-based studies, including epidemiology studies; evaluating the cost/benefit of new and old technology to improve health care in the face of constraints.

IT'S A DOUBLE-EDGE. Scientists have made remarkable progress and they stand on the edge of many more significant discoveries. AHFMR itself stands on the edge. Will it merely maintain existing programs or will the magnitude of the original dream survive? Will Alberta have a world-class community of scientists doing the highest quality research, translated into patient care and economic opportunities?

Will Alberta reap all the benefits from a bold experiment that has worked very well so far—benefits for Albertans and people everywhere?

"There is no doubt in my mind, without an increase in the endowment, we cannot consolidate our gains and see the full fruits of our scientists' achievements. We will be unable to recruit sufficient numbers of first-class talent to fill in the gaps and be unable to pursue new directions as scientists make discoveries and as the problems of patients change. Considering that scientists around the world look to Alberta with envy and praise, it would be a great loss not to capitalize on the unique opportunities created by the Foundation."

Dr. Lionel McLeod,
President, AHFMR

A Story of Achievement

1980-81

First Scholars in place (13)
Training program initiated — 74 Fellows
First 100 students funded
First university renovation grants

1982

197 equipment grants since inception
First Heritage Medical Scientist appointed
Cell Regulation Group formed
1000th application processed

1983

U of C Cardiac Group established
Canada's first Clinical Investigators funded
Nuclear Resonance Program begun
49 senior scientists in place (Heritage Medical
Scientists, Scholars & Clinical Investigators

1984

First AHFMR Fellow becomes a Scholar
Three new specialty clinics established by AHFMR
personnel (Alzheimer's, Sleep Disorders & Obesity)
70 senior scientists in place
New research thrusts in viruses, autism & nutrition

1985

Technology Transfer Program created
87 senior scientists in place (Heritag
Scientists, Scholars & Clinical In
Clinical program thriving
and 8 Investigators
Genetics of Ca
5,000th a

The Science

1980-81

$300 M endowment from Heritage Fund set up
$5.1 M for scientific programs
$13.1 M for scientific programs

1982

$21.6 M for scientific programs

1983

$27.6 M for scientific programs

1984

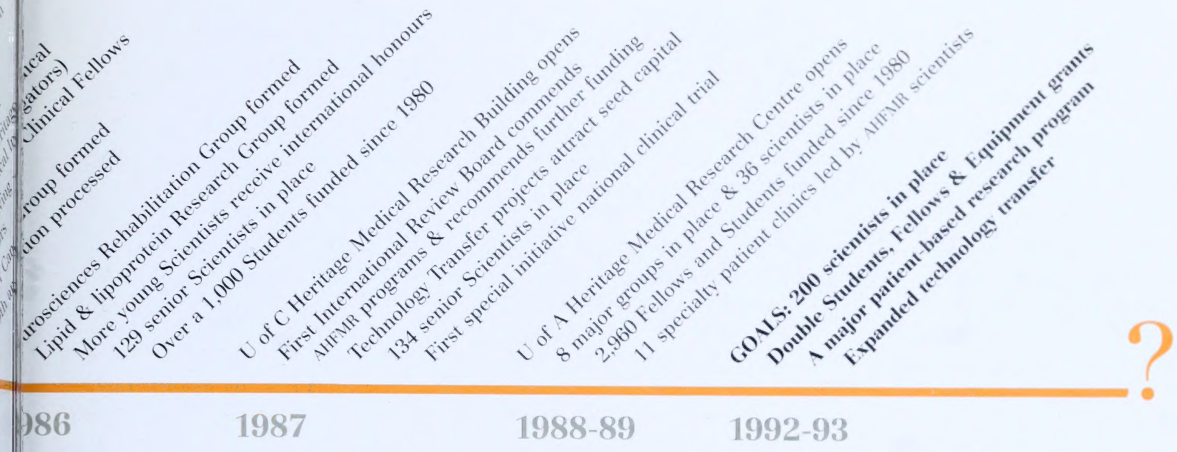
Cumulative funding reaches **$100 M**
Technology Transfer Program established
($600,000 per year)
$32.7 M for scientific programs

1985

Major equipment to university lab reaches $
$38.4 M for scientific programs

*M - $ in millions

The Expenditures



986

ical
gators)
Clinical Fellows
roup formed
ion processed
uroscience Rehabilitation Group formed
Lipid & lipoprotein Research Group formed
More young Scientists receive international honours
129 senior Scientists in place
Over a 1,000 Students funded since 1980

1987

U of C Heritage Medical Research Building opens
First International Review Board commends
AHFMR programs & recommends further funding
Technology Transfer projects attract seed capital
134 senior Scientists in place
First special initiative national clinical trial

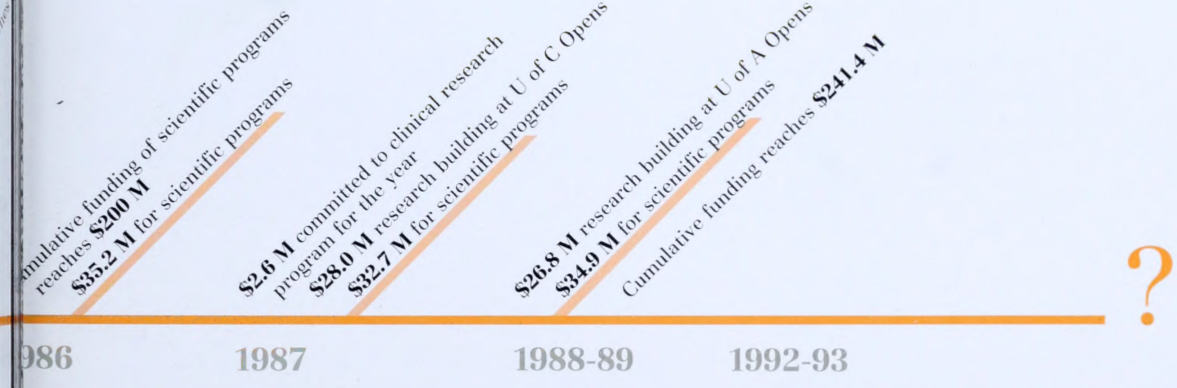
1988-89

U of A Heritage Medical Research Centre opens
8 major groups in place & 36 scientists in place
2,960 Fellows and Students funded since 1980
11 specialty patient clinics led by AHFMR scientists

1992-93

GOALS: 200 scientists in place
Double Students, Fellows & Equipment grants
A major patient-based research program
Expanded technology transfer

?



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mulative funding of scientific programs
reaches **$200 M**
$35.2 M for scientific programs

1987

$2.6 M committed to clinical research
program for the year
$28.0 M research building at U of C Opens
$32.7 M for scientific programs

1988-89

$26.8 M research building at U of A Opens
$34.9 M for scientific programs
Cumulative funding reaches **$241.4 M**

1992-93

?

> *"Based on our conviction that these programs, in their steady state, would support about 200 Scholars, Scientists and Clinical Investigators, we strongly recommend that every effort be made to increase the Endowment of the* AHFMR *to the appropriate level as soon as possible."*
>
> IBR Report 1987

What others say about AHFMR

"What has occurred in Alberta is just wonderful.... It's an example to the rest of Canada—the development of the physical resources and the support to bring people there."

Dr. Har Khorana,
Nobel Laureate in Medicine & Alfred P. Sloan Professor of Biology and Chemistry, MIT, Cambridge, Massachusetts

"The programs of the Foundation have provided a unique medical research milieu that is likely not matched elsewhere in the world. Preserve and strengthen it at all costs."

Dr. Jack Laidlaw,
Executive-Director, (Medical Affairs) Canadian Cancer Society, Toronto

"There's no question that the Foundation has helped put biomedical research in the province on the map. The ability to compete with the strongest institutions for outstanding young scientists has always been limited by the inability of an institution to provide the right intellectual environment on one hand and the right resources of the other. Alberta's two medical schools have been able to match, and in some cases, more than match the best offers anywhere else, including the United States.

I realize the challenge of giving money away wisely and I think the Foundation has done a magnificent job by supporting the best of science in a restricted area and by using most resources to support fundamental research in the conviction that ultimately will result in the most important developments for Alberta's future health care and the public good."

Dr. Maxwell Cowan,
Vice-President & Chief Scientific Officer, Howard Hughes Medical Institute, Seattle

"From our national perspective, the activities of the Foundation are of paramount importance to the growth and maintenance of first class clinical research in Canada, and indirectly to the provision of a high quality of health to all Canadians. The Foundation has shown imagination and leadership."

Dr. Matthew Spence,
President, Canadian Society for Clinical Investigation & Professor of Pediatrics & Biochemistry, Dalhousie University

"In my view the Foundation has had an extraordinary impact on the quality and quantity of science now possible in the two medical schools in Alberta. The visibility and recognition of Alberta's environment has, I think, improved other departments not directly funded by the money, so there are advantages that way as well."

Dr. Joe Martin,
Professor & Chief of Neurology Service, Massachusetts General Hospital, SAC member.

"When I was in Oxford 10 years ago you never heard the word Edmonton and Calgary mentioned by anybody, but it's now become a frequent point of discussion when you're talking about Canadian science."

Dr. John Bell,
Sr. Lecturer, Institute of Molecular Biology, Oxford, England and former AHFMR Fellow.